

97625  
**SEARCH REQUEST FORM**

Requestor's Name: Irene Marx Serial Number: 10/059774  
Date: 6/26/03 Phone: 308-2922 Art Unit: 1651

**Search Topic:**

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

please search inventors

please search process of making enantiopure

1,3 dioxolan-4-one } as in cl. 1  
1,3 <sup>this</sup> dioxolan-5-one }  
A

- Bioconversion of compounds of cl. 2

- with enzyme

- with lipase or esterase

**STAFF USE ONLY**

Date completed: 6/27  
Searcher: Hanley  
Terminal time: 50  
Elapsed time: 60  
CPU time: \_\_\_\_\_  
Total time: \_\_\_\_\_  
Number of Searches: \_\_\_\_\_  
Number of Databases: \_\_\_\_\_

Search Site  
\_\_\_\_ STIC  
\_\_\_\_ CM-1  
\_\_\_\_ Pre-S  
Type of Search  
\_\_\_\_ N.A. Sequence  
\_\_\_\_ A.A. Sequence  
\_\_\_\_ 1 Structure  
\_\_\_\_ Bibliographic

Vendors  
\_\_\_\_ IG  
536 STN  
\_\_\_\_ Dialog  
\_\_\_\_ APS  
\_\_\_\_ Geninfo  
\_\_\_\_ SDC  
\_\_\_\_ DARC/Questel  
\_\_\_\_ Other

# Inventor search

MARX 10/059,774

=> d que l12

L1 77 SEA FILE=HCAPLUS ABB=ON PLU=ON POPP A?/AU  
L2 30 SEA FILE=HCAPLUS ABB=ON PLU=ON STOHRER J?/AU  
L3 780 SEA FILE=HCAPLUS ABB=ON PLU=ON PETERSEN H?/AU  
L4 3 SEA FILE=HCAPLUS ABB=ON PLU=ON GILCH A?/AU  
L5 4 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ROCKINGER MECHLEM JODOCA"/AU  
OR "ROCKINGHAM C J"/AU)  
L6 883 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5)  
L7 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND ?DIOXOLAN?  
L8 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND ?OXATHIOLAN?  
L10 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L7 OR L8)  
L11 23 SEA FILE=REGISTRY ABB=ON PLU=ON (107053-35-0/BI OR 146528-24-  
7/BI OR 1634-04-4/BI OR 166116-95-6/BI OR 4158-81-0/BI OR  
4385-46-0/BI OR 444730-15-8/BI OR 444730-16-9/BI OR 444730-17-0  
/BI OR 444730-18-1/BI OR 444730-19-2/BI OR 444730-20-5/BI OR  
444730-21-6/BI OR 444730-22-7/BI OR 444730-23-8/BI OR 444730-24  
-9/BI OR 444730-25-0/BI OR 64-17-5/BI OR 67-56-1/BI OR  
75-05-8/BI OR 7732-18-5/BI OR 9001-62-1/BI OR 9016-18-6/BI)  
L12 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L10

*1 cite*

=&gt; d ibib abs hitstr ind

L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:591755 HCAPLUS

DOCUMENT NUMBER: 137:139499

TITLE: Method for the enzymatic preparation of enantiomerically pure derivatives of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one

INVENTOR(S): Popp, Alfred; Stohrer, Juergen; Petersen, Hermann; Gilch, Andrea; Rockinger-Mechlem, Jodoca

PATENT ASSIGNEE(S): Consortium Fuer Elektrochemische Industrie GmbH, Germany

SOURCE: Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229127	A1	20020807	EP 2002-1124	20020124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
DE 10104231	A1	20020808	DE 2001-10104231	20010131
JP 2002281997	A2	20021002	JP 2002-22091	20020130

PRIORITY APPLN. INFO.: DE 2001-10104231 A 20010131

OTHER SOURCE(S): CASREACT 137:139499; MARPAT 137:139499

AB A process is provided for the prodn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by an enzyme mediated kinetic resoln. of a racemate. When a racemic 1,3-dioxolan-4-one or 1,3-oxathiolan-5-one deriv. is mixed with a lipase or esterase in the presence of an oxygen contg. nucleophile, the dioxolane/ oxathiolane ring of one enantiomer is hydrolyzed at faster rate than the other enantiomer. Thus, 2-methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is mixed with Novozym 435 (a com. lipase) and methanol, (+)-(R)-2-Methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is produced with an enantiomeric excess > 98%.

IT 1634-04-4, MTBE

RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process) (prepn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)

RN 1634-04-4 HCAPLUS

CN Propane, 2-methoxy-2-methyl- (9CI) (CA INDEX NAME)

t-Bu-O-Me

IT 4158-81-ODP, 1,3-Dioxolan-4-one, and derivs. of 4385-46-ODP, 1,3-Oxathiolan-5-one, and derivs. of

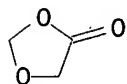
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(prepn. of enantiomerically pure derivs. of 1,3-dioxolan

-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)

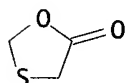
RN 4158-81-0 HCAPLUS

CN 1,3-Dioxolan-4-one (8CI, 9CI) (CA INDEX NAME)



RN 4385-46-0 HCAPLUS

CN 1,3-Oxathiolan-5-one (8CI, 9CI) (CA INDEX NAME)



IT 9001-62-1, Lipase 9016-18-6, Esterase, carboxyl

RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)

(prepn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)

RN 9001-62-1 HCAPLUS

CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9016-18-6 HCAPLUS

CN Esterase, carboxyl (8CI, 9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 444730-15-8P 444730-17-0P 444730-18-1P

444730-19-2P 444730-21-6P 444730-23-8P

444730-25-0P

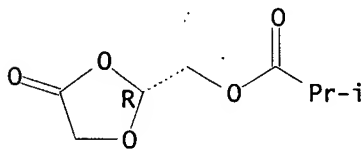
RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)

(prepn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)

RN 444730-15-8 HCAPLUS

CN Propanoic acid, 2-methyl-, [(2R)-4-oxo-1,3-dioxolan-2-yl]methyl ester (9CI) (CA INDEX NAME)

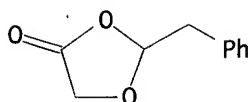
Absolute stereochemistry. Rotation (+).



RN 444730-17-0 HCAPLUS

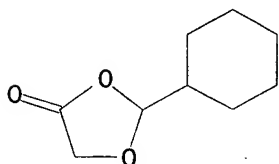
CN 1,3-Dioxolan-4-one, 2-(phenylmethyl)-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



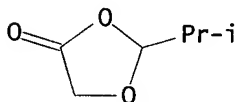
RN 444730-18-1 HCAPLUS  
CN 1,3-Dioxolan-4-one, 2-cyclohexyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



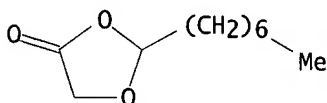
RN 444730-19-2 HCAPLUS  
CN 1,3-Dioxolan-4-one, 2-(1-methylethyl)-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



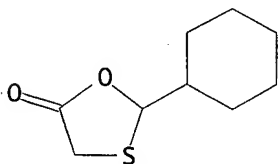
RN 444730-21-6 HCAPLUS  
CN 1,3-Dioxolan-4-one, 2-heptyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



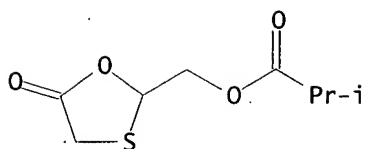
RN 444730-23-8 HCAPLUS  
CN 1,3-Oxathiolan-5-one, 2-cyclohexyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

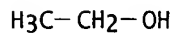


RN 444730-25-0 HCAPLUS  
CN Propanoic acid, 2-methyl-, (5-oxo-1,3-oxathiolan-2-yl)methyl ester, (+)- (9CI) (CA INDEX NAME)

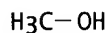
Rotation (+).



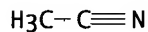
IT 64-17-5, Ethanol, reactions 67-56-1, Methanol, reactions 75-05-8, Acetonitrile, reactions 7732-18-5, Water, reactions 107053-35-0 146528-24-7 166116-95-6 444730-16-9 444730-20-5 444730-22-7 444730-24-9  
 RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
 (prepn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)  
 RN 64-17-5 HCAPLUS  
 CN Ethanol (9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS  
 CN Methanol (8CI, 9CI) (CA INDEX NAME)



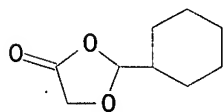
RN 75-05-8 HCAPLUS  
 CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)



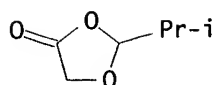
RN 7732-18-5 HCAPLUS  
 CN Water (8CI, 9CI) (CA INDEX NAME)



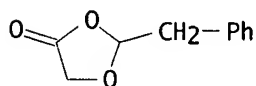
RN 107053-35-0 HCAPLUS  
 CN 1,3-Dioxolan-4-one, 2-(1-methylethoxy)- (9CI) (CA INDEX NAME)



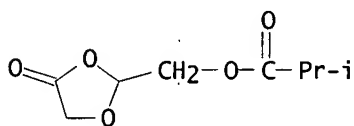
RN 146528-24-7 HCAPLUS  
 CN 1,3-Dioxolan-4-one, 2-(1-methylethoxy)- (9CI) (CA INDEX NAME)



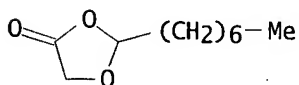
RN 166116-95-6 HCAPLUS  
CN 1,3-Dioxolan-4-one, 2-(phenylmethyl)- (9CI) (CA INDEX NAME)



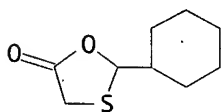
RN 444730-16-9 HCAPLUS  
CN Propanoic acid, 2-methyl-, (4-oxo-1,3-dioxolan-2-yl)methyl ester (9CI)  
(CA INDEX NAME)



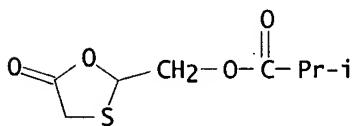
RN 444730-20-5 HCAPLUS  
CN 1,3-Dioxolan-4-one, 2-heptyl- (9CI) (CA INDEX NAME)



RN 444730-22-7 HCAPLUS  
CN 1,3-Oxathiolan-5-one, 2-cyclohexyl- (9CI) (CA INDEX NAME)



RN 444730-24-9 HCAPLUS  
CN Propanoic acid, 2-methyl-, (5-oxo-1,3-oxathiolan-2-yl)methyl ester (9CI)  
(CA INDEX NAME)



IC ICM C12P041-00  
CC 16-5 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 28

- ST enzymic kinetic resolu **dioxolane oxathiolane** deriv
- IT Columns and Towers  
(bioreactor; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Bioreactors  
(column; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Enzymes, uses  
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)  
(com.; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Resolution (separation)  
(enzymic, kinetic; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Hydrolysis  
(enzymic, stereoselective; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Hydrocarbons, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
(halo; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Enzymes, uses  
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)  
(immobilized; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Ring opening  
(nucleophilic; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Nucleophiles  
(oxygen contg.; prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Distillation  
Extraction  
Temperature  
(prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Ethers, preparation  
RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)  
(prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Alcohols, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
(prepn. of enantiomerically pure derivs. of 1,3-**dioxolan-4-one** and 1,3-**oxathiolan-5-one** by enzymic kinetic resolu.)
- IT Aromatic hydrocarbons, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)



- (prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT Esters, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT Hydrocarbons, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT Alcohols, reactions  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(secondary; prepn. of enantiomerically pure derivs. of 1,3-  
dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic  
kinetic resoln.)
- IT Bioreactors  
(stirred-tank; prepn. of enantiomerically pure derivs. of 1,3-  
dioxolan-4-one and 1,3-oxathiolan-5-one by enzymic  
kinetic resoln.)
- IT 1634-04-4, MTBE  
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT 4158-81-ODP, 1,3-Dioxolan-4-one, and derivs. of  
4385-46-ODP, 1,3-Oxathiolan-5-one, and derivs. of  
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); BPN  
(Biosynthetic preparation); PUR (Purification or recovery); RCT  
(Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process);  
RACT (Reactant or reagent)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT 9001-62-1, Lipase 9016-18-6, Esterase, carboxyl  
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological  
study); PROC (Process); USES (Uses)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT 444730-15-8P 444730-17-0P 444730-18-1P  
444730-19-2P 444730-21-6P 444730-23-8P  
444730-25-0P  
RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL  
(Biological study); PREP (Preparation); PROC (Process)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- IT 64-17-5, Ethanol, reactions 67-56-1, Methanol, reactions  
75-05-8, Acetonitrile, reactions 7732-18-5, Water,  
reactions 107053-35-0 146528-24-7 166116-95-6  
444730-16-9 444730-20-5 444730-22-7  
444730-24-9  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(prepn. of enantiomerically pure derivs. of 1,3-dioxolan  
-4-one and 1,3-oxathiolan-5-one by enzymic kinetic resoln.)
- REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

# Inventor search

MARX 10/059,774

=> d que 116

L1 77 SEA FILE=HCAPLUS ABB=ON PLU=ON POPP A?/AU  
L2 30 SEA FILE=HCAPLUS ABB=ON PLU=ON STOHRER J?/AU  
L3 780 SEA FILE=HCAPLUS ABB=ON PLU=ON PETERSEN H?/AU  
L4 3 SEA FILE=HCAPLUS ABB=ON PLU=ON GILCH A?/AU  
L5 4 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ROCKINGER MECHLEM JODOCA"/AU  
OR "ROCKINGHAM C J"/AU)  
L6 883 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5)  
L7 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND ?DIOXOLAN?  
L8 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND ?OXATHIOLAN?  
L9 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND ENANTIO?  
L10 1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L7 OR L8)  
L13 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 NOT L10  
L14 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (ENZYM? OR LIPASE OR  
ESTERASE)  
L15 19 SEA FILE=REGISTRY ABB=ON PLU=ON (1634-04-4/BI OR 215316-59-9/  
BI OR 385812-12-4/BI OR 503322-41-6/BI OR 503322-42-7/BI OR  
503322-43-8/BI OR 503322-44-9/BI OR 503322-45-0/BI OR 503322-46  
-1/BI OR 503322-47-2/BI OR 503322-48-3/BI OR 503322-49-4/BI OR  
503322-50-7/BI OR 503322-51-8/BI OR 503322-52-9/BI OR 503441-37  
-0/BI OR 9001-62-1/BI OR 9016-18-6/BI OR 94064-20-7/BI)  
L16 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L15

*1 citation*

=&gt; d ibib abs hitstr ind

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:259778 HCAPLUS

DOCUMENT NUMBER: 138:270415

TITLE: Lipase catalyzed kinetic resolution of

.beta.-hydroxy carboxylic acid esters

INVENTOR(S): Popp, Alfred; Petersen, Hermann;  
Stohrer, Juergen; Rockinger-Mechlem,  
Jodoca; Gilch, AndreaPATENT ASSIGNEE(S): Consortium Fuer Elektrochemische Industrie G.m.b.H.,  
Germany

SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1298218	A1	20030402	EP 2002-21271	20020919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
DE 10147653	A1	20030424	DE 2001-10147653	20010927
US 2003109029	A1	20030612	US 2002-255776	20020926

PRIORITY APPLN. INFO.: DE 2001-10147653 A 20010927

OTHER SOURCE(S): CASREACT 138:270415; MARPAT 138:270415

AB A process is provided for the prodn. of **enantiomerically** pure .beta.-hydroxycarboxylic acids by **enzymic** kinetic resoln. of a racemic mixt. Thus, racemic Me 3-hydroxy-5-phenyl-3-propyl-(E)-4-pentenoate was kinetically resolved at pH 8.0 with Novozyme.RTM. 525F to yield the R **enantiomer**. The aq. reaction mixt. was extd. with Me tert-Bu ether (MBTE), filtered through sodium sulfate and concd. under vacuum. The residue contained (R)-(+)-Me 3-hydroxy-5-phenyl-3-propyl-(E)-4-pentenoate with an **enantiomeric** excess of 72%. The remaining aq. phase was acidified to pH 2.0 and extd. with MBTE and the org. phase was also filtered through sodium sulfate and concd. under vacuum. The residue from this extn. yielded (S)-(-)-3-hydroxy-5-phenyl-3-propyl-(E)-4-pentenoic acid with an **enantiomeric** excess of 96%.

IT 9001-62-1, Lipase

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);

PROC (Process); RACT (Reactant or reagent)

(Novozyme 525F; lipase catalyzed kinetic resoln. of

.beta.-hydroxy carboxylic acid esters)

RN 9001-62-1 HCAPLUS

CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 503322-42-7P 503322-45-0P 503322-47-2P

503322-49-4P 503322-52-9P

RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL

(Biological study); PREP (Preparation); PROC (Process)

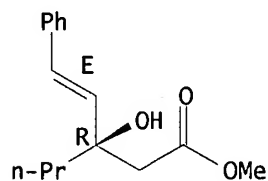
(lipase catalyzed kinetic resoln. of .beta.-hydroxy

carboxylic acid esters)

RN 503322-42-7 HCAPLUS

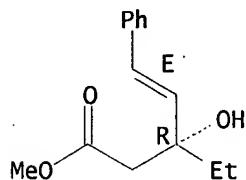
CN Hexanoic acid, 3-hydroxy-3-[(1E)-2-phenylethenyl]-, methyl ester, (3R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



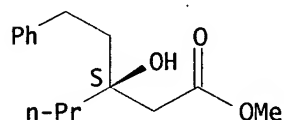
RN 503322-45-0 HCAPLUS  
CN 4-Pentenoic acid, 3-ethyl-3-hydroxy-5-phenyl-, methyl ester, (3R,4E)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



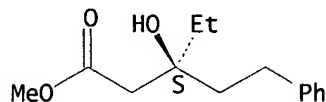
RN 503322-47-2 HCAPLUS  
CN Benzenepentanoic acid, .beta.-hydroxy-.beta.-propyl-, methyl ester,  
(.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



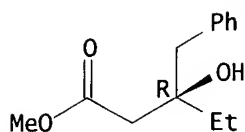
RN 503322-49-4 HCAPLUS  
CN Benzenepentanoic acid, .beta.-ethyl-.beta.-hydroxy-, methyl ester,  
(.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 503322-52-9 HCAPLUS  
CN Benzenebutanoic acid, .beta.-ethyl-.beta.-hydroxy-, methyl ester,  
(.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9016-18-6, Carboxy esterase 385812-12-4

503322-41-6 503322-44-9 503322-48-3

503322-51-8

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);

PROC (Process); RACT (Reactant or reagent)

(lipase catalyzed kinetic resoln. of .beta.-hydroxy  
carboxylic acid esters)

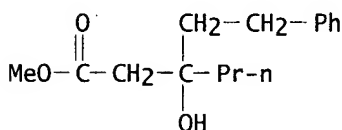
RN 9016-18-6 HCAPLUS

CN Esterase, carboxyl (8CI, 9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 385812-12-4 HCAPLUS

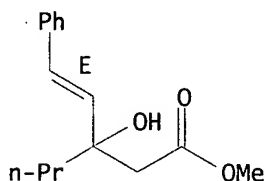
CN Benzenepentanoic acid, .beta.-hydroxy-.beta.-propyl-, methyl ester (9CI)  
(CA INDEX NAME)



RN 503322-41-6 HCAPLUS

CN Hexanoic acid, 3-hydroxy-3-[(1E)-2-phenylethenyl]-, methyl ester (9CI)  
(CA INDEX NAME)

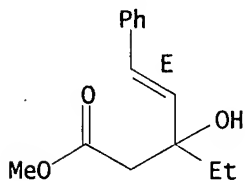
Double bond geometry as shown.



RN 503322-44-9 HCAPLUS

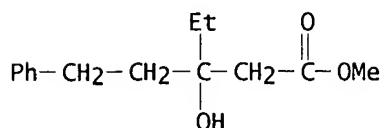
CN 4-Pentenoic acid, 3-ethyl-3-hydroxy-5-phenyl-, methyl ester, (4E)- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



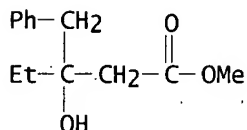
RN 503322-48-3 HCAPLUS

CN Benzenepentanoic acid, .beta.-ethyl-.beta.-hydroxy-, methyl ester (9CI)  
(CA INDEX NAME)



RN 503322-51-8 HCAPLUS

CN Benzenebutanoic acid, .beta.-ethyl-.beta.-hydroxy-, methyl ester (9CI)  
(CA INDEX NAME)



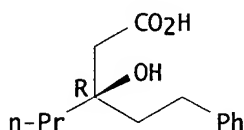
IT 215316-59-9P 503322-43-8P 503322-46-1P  
503322-50-7P 503441-37-0P

RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL  
(Biological study); PREP (Preparation)  
(lipase catalyzed kinetic resoln. of .beta.-hydroxy  
carboxylic acid esters)

RN 215316-59-9 HCAPLUS

CN Benzenepentanoic acid, .beta.-hydroxy-.beta.-propyl-, (.beta.R)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

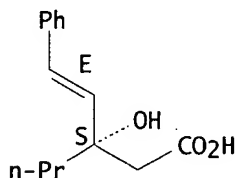


RN 503322-43-8 HCAPLUS

CN Hexanoic acid, 3-hydroxy-3-[(1E)-2-phenylethenyl]-, (3S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry. Rotation (-).

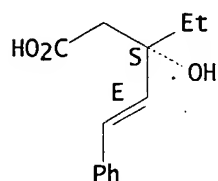
Double bond geometry as shown.



RN 503322-46-1 HCAPLUS

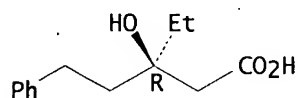
CN 4-Pentenoic acid, 3-ethyl-3-hydroxy-5-phenyl-, (3S,4E)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



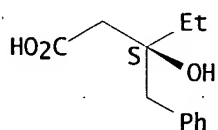
RN 503322-50-7 HCAPLUS  
CN Benzenepentanoic acid, .beta.-ethyl-.beta.-hydroxy-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 503441-37-0 HCAPLUS  
CN Benzenebutanoic acid, .beta.-ethyl-.beta.-hydroxy-, (.beta.S)- (9CI) (CA INDEX NAME)

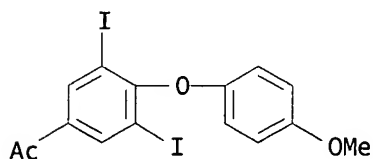
Absolute stereochemistry.



IT 1634-04-4, Methyl tert-butyl ether 94064-20-7, DIPE  
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)  
(lipase catalyzed kinetic resolu. of .beta.-hydroxy carboxylic acid esters)  
RN 1634-04-4 HCAPLUS  
CN Propane, 2-methoxy-2-methyl- (9CI) (CA INDEX NAME)

t-Bu-O-Me

RN 94064-20-7 HCAPLUS  
CN Ethanone, 1-[3,5-diiodo-4-(4-methoxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



- IC ICM C12P041-00  
 CC 16-5 (Fermentation and Bioindustrial Chemistry)  
 Section cross-reference(s): 7  
 ST **lipase** kinetic resoln beta hydroxy carboxylate  
 IT Resolution (separation)  
 (enzymic, kinetic; **lipase** catalyzed kinetic resoln.  
 of .beta.-hydroxy carboxylic acid esters)  
 IT Hydrolysis  
 (enzymic, stereoselective; **lipase** catalyzed kinetic  
 resoln. of .beta.-hydroxy carboxylic acid esters)  
 IT Carboxylic acids, preparation  
 RL: BCP (Biochemical process); PUR (Purification or recovery); RCT  
 (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process);  
 RACT (Reactant or reagent)  
 (esters, .beta.-hydroxy; **lipase** catalyzed kinetic resoln. of  
 .beta.-hydroxy carboxylic acid esters)  
 IT Carboxylic acids, preparation  
 RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL  
 (Biological study); PREP (Preparation)  
 (hydroxy; **lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)  
 IT Distillation  
 Esterification  
 Extraction  
 Saponification  
 (**lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)  
 IT Temperature  
 (range for the reaction, 20-50 .degree.C; **lipase** catalyzed  
 kinetic resoln. of .beta.-hydroxy carboxylic acid esters)  
 IT 9001-62-1, **Lipase**  
 RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
 PROC (Process); RACT (Reactant or reagent)  
 (Novozyme 525F; **lipase** catalyzed kinetic resoln. of  
 .beta.-hydroxy carboxylic acid esters)  
 IT 503322-42-7P 503322-45-0P 503322-47-2P  
 503322-49-4P 503322-52-9P  
 RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL  
 (Biological study); PREP (Preparation); PROC (Process)  
 (**lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)  
 IT 9016-18-6, Carboxy **esterase** 385812-12-4  
 503322-41-6 503322-44-9 503322-48-3  
 503322-51-8  
 RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
 PROC (Process); RACT (Reactant or reagent)  
 (**lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)  
 IT 215316-59-9P 503322-43-8P 503322-46-1P  
 503322-50-7P 503441-37-0P  
 RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL  
 (Biological study); PREP (Preparation)  
 (**lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)  
 IT 1634-04-4, Methyl tert-butyl ether 94064-20-7, DIPE  
 RL: CPS (Chemical process); PEP (Physical, engineering or chemical  
 process); PROC (Process)  
 (**lipase** catalyzed kinetic resoln. of .beta.-hydroxy  
 carboxylic acid esters)



MARX 10/059,774

REFERENCE COUNT:

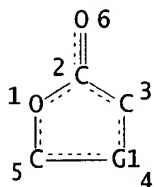
6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

# Registry & HCAPLUS Search

MARX 10/059,774

=> D QUE L22 STAT  
L19 STR  
S @7

← STR for all searches in HCAPLUS



← ring can be fused

VAR G1=O/7  
NODE ATTRIBUTES:  
CONNECT IS E2 RC AT 7  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE  
L22 3939 SEA FILE=REGISTRY SSS FUL L19 3,939 compounds

100.0% PROCESSED 13822 ITERATIONS  
SEARCH TIME: 00.00.01

3939 ANSWERS

=&gt; D QUE NOS L33

L19 STR *← STR on previous page*  
 L22 3939 SEA FILE=REGISTRY SSS FUL L19 *3,939 compounds*  
 L23 1 SEA FILE=REGISTRY ABB=ON PLU=ON LIPASE/CN  
 L24 2 SEA FILE=REGISTRY ABB=ON PLU=ON ESTERASE/CN  
 L25 1396 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 *cites for compounds*  
 L26 33389 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 OR LIPASE/OBI  
 L27 25940 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 OR ESTERASE/OBI  
 L28 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND (L26 OR L27)  
 L31 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND ENZYM?/OBI  
 L32 18115 SEA FILE=HCAPLUS ABB=ON PLU=ON "RESOLUTION (SEPARATION)" +PFT,  
 NT/CT  
 L33 4 SEA FILE=HCAPLUS ABB=ON PLU=ON (L28 OR L31) AND L32 *4 cites*

=&gt; D QUE NOS L35

L19 STR  
 L22 3939 SEA FILE=REGISTRY SSS FUL L19  
 L23 1 SEA FILE=REGISTRY ABB=ON PLU=ON LIPASE/CN  
 L24 2 SEA FILE=REGISTRY ABB=ON PLU=ON ESTERASE/CN  
 L25 1396 SEA FILE=HCAPLUS ABB=ON PLU=ON L22  
 L26 33389 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 OR LIPASE/OBI  
 L27 25940 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 OR ESTERASE/OBI  
 L28 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND (L26 OR L27)  
 L31 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND ENZYM?/OBI  
 L34 103924 SEA FILE=HCAPLUS ABB=ON PLU=ON (RESOLUTION OR RESOLV?)/OBI  
 L35 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND (L28 OR L31) *7 cites*

=&gt; D QUE NOS L36

L19 STR  
 L22 3939 SEA FILE=REGISTRY SSS FUL L19  
 L23 1 SEA FILE=REGISTRY ABB=ON PLU=ON LIPASE/CN  
 L24 2 SEA FILE=REGISTRY ABB=ON PLU=ON ESTERASE/CN  
 L25 1396 SEA FILE=HCAPLUS ABB=ON PLU=ON L22  
 L26 33389 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 OR LIPASE/OBI  
 L27 25940 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 OR ESTERASE/OBI  
 L28 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND (L26 OR L27)  
 L31 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND ENZYM?/OBI  
 L36 3 SEA FILE=HCAPLUS ABB=ON PLU=ON (L28 OR L31) AND ENANTIO?/OBI *3 cites*

=&gt; S L33 OR L35 OR L36

L45 8 L33 OR L35 OR L36 *8 cites total*

CT = controlled  
 terminology  
 PFT = old, new or  
 "used for" terms  
 NT = narrower terms  
 OBI = all fields  
 except the  
 abstract

=&gt; d ibib abs hitstr 1-8.L45

L45 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:591755 HCAPLUS

DOCUMENT NUMBER: 137:139499

TITLE: Method for the enzymatic preparation of

**enantiomerically** pure derivatives of

1,3-dioxolan-4-one and 1,3-oxathiolan-5-one

INVENTOR(S): Popp, Alfred; Stohrer, Juergen; Petersen, Hermann;

Gilch, Andrea; Rockinger-Mechlem, Jodoca

PATENT ASSIGNEE(S): Consortium Fuer Elektrochemische Industrie GmbH,

Germany

SOURCE: Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229127	A1	20020807	EP 2002-1124	20020124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
DE 10104231	A1	20020808	DE 2001-10104231	20010131
JP 2002281997	A2	20021002	JP 2002-22091	20020130

PRIORITY APPLN. INFO.: DE 2001-10104231 A 20010131

OTHER SOURCE(S): CASREACT 137:139499; MARPAT 137:139499

AB A process is provided for the prodn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by an enzyme mediated kinetic resoln. of a racemate. When a racemic 1,3-dioxolan-4-one or 1,3-oxathiolan-5-one deriv. is mixed with a lipase or esterase in the presence of an oxygen contg. nucleophile, the dioxolane/ oxathiolane ring of one enantiomer is hydrolyzed at faster rate than the other enantiomer. Thus, 2-methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is mixed with Novozym 435 (a com. lipase) and methanol, (+)-(R)-2-Methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is produced with an enantiomeric excess > 98%.

IT 4158-81-ODP, 1,3-Dioxolan-4-one, and derivs. of

4385-46-ODP, 1,3-Oxathiolan-5-one, and derivs. of

RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); BPN

(Biosynthetic preparation); PUR (Purification or recovery); RCT

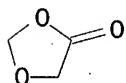
(Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process);

RACT (Reactant or reagent)

(prepn. of **enantiomerically** pure derivs. of1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by **enzymic**kinetic **resoln.**)

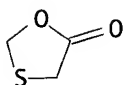
RN 4158-81-0 HCAPLUS

CN 1,3-Dioxolan-4-one (8CI, 9CI) (CA INDEX NAME)



RN 4385-46-0 HCAPLUS

CN 1,3-Oxathiolan-5-one (8CI, 9CI) (CA INDEX NAME)



IT 9001-62-1, Lipase 9016-18-6, Esterase

, carboxyl

RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)

(prepn. of **enantiomerically** pure derivs. of  
1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by **enzymic**  
kinetic **resoln.**)

RN 9001-62-1 HCAPLUS

CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9016-18-6 HCAPLUS

CN Esterase, carboxyl (8CI, 9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 444730-15-8P 444730-17-0P 444730-18-1P

444730-19-2P 444730-21-6P 444730-23-8P

444730-25-0P

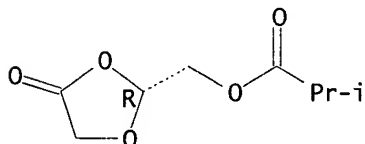
RL: BCP (Biochemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)

(prepn. of **enantiomerically** pure derivs. of  
1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by **enzymic**  
kinetic **resoln.**)

RN 444730-15-8 HCAPLUS

CN Propanoic acid, 2-methyl-, [(2R)-4-oxo-1,3-dioxolan-2-yl]methyl ester (9CI) (CA INDEX NAME)

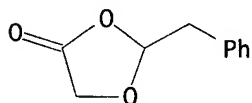
Absolute stereochemistry. Rotation (+).



RN 444730-17-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(phenylmethyl)-, (+)- (9CI) (CA INDEX NAME)

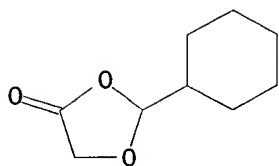
Rotation (+).



RN 444730-18-1 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-cyclohexyl-, (+)- (9CI) (CA INDEX NAME)

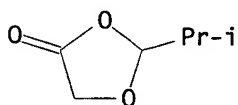
Rotation (+).



RN 444730-19-2 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1-methylethyl)-, (+)- (9CI) (CA INDEX NAME)

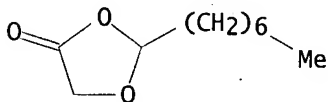
Rotation (+).



RN 444730-21-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-heptyl-, (+)- (9CI) (CA INDEX NAME)

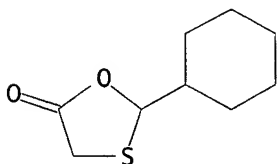
Rotation (+).



RN 444730-23-8 HCAPLUS

CN 1,3-Oxathiolan-5-one, 2-cyclohexyl-, (+)- (9CI) (CA INDEX NAME)

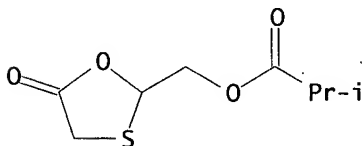
Rotation (+).



RN 444730-25-0 HCAPLUS

CN Propanoic acid, 2-methyl-, (5-oxo-1,3-oxathiolan-2-yl)methyl ester, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



IT 107053-35-0 146528-24-7 166116-95-6

444730-16-9 444730-20-5 444730-22-7

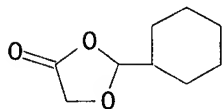
444730-24-9

MARX 10/059,774

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(prepn. of **enantiomerically** pure derivs. of  
1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by **enzymic**  
kinetic **resoln.**)

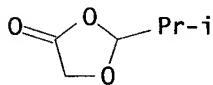
RN 107053-35-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-cyclohexyl- (9CI) (CA INDEX NAME)



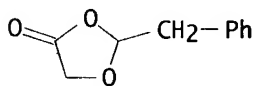
RN 146528-24-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1-methylethyl)- (9CI) (CA INDEX NAME)



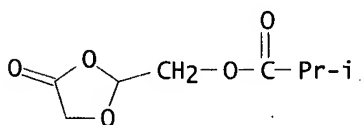
RN 166116-95-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(phenylmethyl)- (9CI) (CA INDEX NAME)



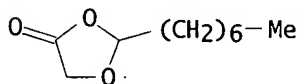
RN 444730-16-9 HCAPLUS

CN Propanoic acid, 2-methyl-, (4-oxo-1,3-dioxolan-2-yl)methyl ester (9CI)  
(CA INDEX NAME)



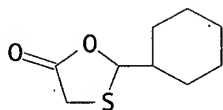
RN 444730-20-5 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-heptyl- (9CI) (CA INDEX NAME)

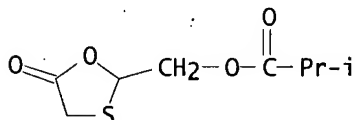


RN 444730-22-7 HCAPLUS

CN 1,3-Oxathiolan-5-one, 2-cyclohexyl- (9CI) (CA INDEX NAME)



RN 444730-24-9 HCAPLUS  
 CN Propanoic acid, 2-methyl-, (5-oxo-1,3-oxathiolan-2-yl)methyl ester (9CI)  
 (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE. FORMAT

L45 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:51415 HCAPLUS

DOCUMENT NUMBER: 136:118468

TITLE: Preparation of 2-aryl-2-hydroxyacetic acid ester derivatives as muscarinic M3 receptor antagonists  
 INVENTOR(S): Ogino, Yoshio; Kurihara, Hideki; Matsuda, Kenji; Numazawa, Tomoshige; Otake, Norikazu; Noguchi, Kazuhito

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004402	A1	20020117	WO 2001-JP5987	20010710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001071027	A5	20020121	AU 2001-71027	20010710
EP 1302458	A1	20030416	EP 2001-949925	20010710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:		JP 2000-210591 A 20000711		
		WO 2001-JP5987 W 20010710		

OTHER SOURCE(S): MARPAT 136:118468

AB Compds. of the general formula  $\text{ArC(OH)(R1)CO2A}$  [wherein A is a group of the general formula  $-\text{B1}-\text{N}^+\text{R2R3R4.X}^-$  or  $-\text{B2}-\text{NR5CR6:NR7}$ ; Ar is aryl or heteroaryl, any of which may be substituted; B1 and B2 are each an aliph.



hydrocarbon group; R1 is fluorinated cycloalkyl; R2, R3 and R4 are each lower alkyl, or a single bond or alkylene, any of which is bonded to B1, or alternatively R2 and R3 may be united to form alkylene; R5 and R7 are each hydrogen, lower alkyl, or a single bond or alkylene, any of which is bonded to B2; R6 is hydrogen, lower alkyl, or N(R8)R9; R8 and R9 are independently hydrogen or lower alkyl; and X- is an anion] are prepd. These compds. exhibit selective muscarinic M3 receptor antagonism with little side effects and are suitable for administration by inhalation and useful as therapeutic agents for respiratory system diseases including chronic obstructive pulmonary diseases, chronic bronchitis, asthma, chronic airway obstruction, pulmonary fibrosis, pulmonary emphysema, or rhinitis. Thus, reductive methylation of piperidin-4-yl (2R)-((1R)-3,3-difluoropentyl)-2-hydroxy-2-phenylethanoate by formaldehyde and sodium cyanoborohydride in the presence of ZnCl<sub>2</sub> in MeOH at room temp. for 30 min gave 1-methylpiperidin-4-yl (2R)-((1R)-3,3-difluoropentyl)-2-hydroxy-2-phenylethanoate which was quaternized by Me bromide in MeCN at room temp. for 15 h to give 4-[[[(2R)-2-((1R)-3,3-difluorocyclopentyl)-2-hydroxy-2-phenylethanoyl]oxy]-1,1-dimethylpiperidinium bromide (I). In a muscarinic receptor M2 and M3 antagonism assay, 4-(((2R)-2-((1R)-3,3-difluorocyclopentyl)-2-hydroxy-2-phenylethanoyl)oxy)-1,1-dimethylpiperidinium bromide in vitro exhibited KB of 9.6 nM for inhibiting the carbachol-induced redn. in heart beat in rat right atrium (muscarinic receptor M2 receptor) and that of 0.004 nM for inhibiting the carbachol-induced contraction of trachea (muscarinic receptor M3 receptor) with M2/M3 receptor ratio of 218. An ampule or a powder inhalation formulation contg. I were described.

## IT 9001-62-1, Lipase AK

RL: CAT (Catalyst use); USES (Uses)

(enzymic resoln. of 2-(2,4-difluorophenyl)-2-hydroxyacetic acid; prepn. of arylhydroxyacetic acid ester derivs. as muscarinic M3 receptor antagonists)

RN 9001-62-1 HCAPLUS

CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

## IT 116907-30-3, (2R,5R)-2-tert-Butyl-5-phenyl-1,3-dioxolan-4-one

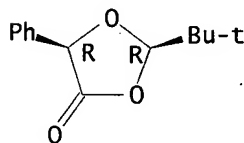
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of arylhydroxyacetic acid ester derivs. as muscarinic M3 receptor antagonists for therapeutic agents)

RN 116907-30-3 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## IT 203321-54-4P, (2R,5R)-2-tert-Butyl-5-((1S)-3-oxocyclopentyl)-5-phenyl-1,3-dioxolan-4-one 203321-55-5P 203321-57-7P

389889-38-7P, (2R,5R)-2-tert-Butyl-5-(4-chlorophenyl)-1,3-dioxolan-4-one 389889-46-7P, (2R,5R)-2-tert-Butyl-5-((1R)-3-hydroxycyclopentyl)-5-phenyl-1,3-dioxolan-4-one 389889-48-9P, (4R)-4-((2R,4R)-2-tert-Butyl-5-oxo-4-phenyl-1,3-dioxolan-4-yl)-1-cyclopentenyl acetate 389889-49-0P, (3R)-3-((2R,4R)-2-tert-Butyl-5-oxo-4-phenyl-1,3-dioxolan-4-yl)-1-cyclopentenyl acetate

**389889-50-3P**, (2R,5R)-2-tert-Butyl-5-((1R,3R)-3-hydroxy-4-oxocyclopentyl)-5-phenyl-1,3-dioxolan-4-one **389889-51-4P**, (1R,4R)-4-((2R,4R)-2-tert-Butyl-5-oxo-4-phenyl-1,3-dioxolan-4-yl)-2-oxocyclopentyl acetate

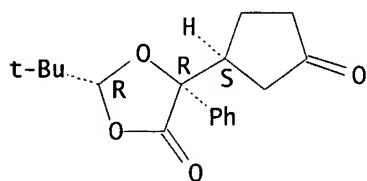
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of arylhydroxyacetic acid ester derivs. as muscarinic M3 receptor antagonists for therapeutic agents)

RN 203321-54-4 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-[(1S)-3-oxocyclopentyl]-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

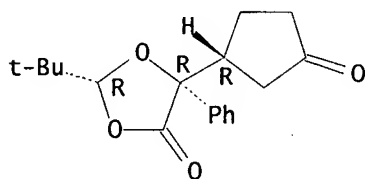
Absolute stereochemistry. Rotation (-).



RN 203321-55-5 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-[(1R)-3-oxocyclopentyl]-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

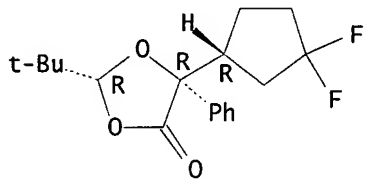
Absolute stereochemistry. Rotation (+).



RN 203321-57-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(1R)-3,3-difluorocyclopentyl]-2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

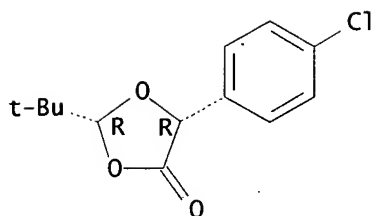
Absolute stereochemistry. Rotation (+).



RN 389889-38-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-chlorophenyl)-2-(1,1-dimethylethyl)-, (2R,5R)- (9CI) (CA INDEX NAME)

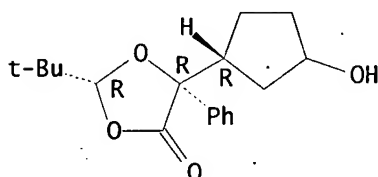
Absolute stereochemistry.



RN 389889-46-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-[(1R)-3-hydroxycyclopentyl]-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

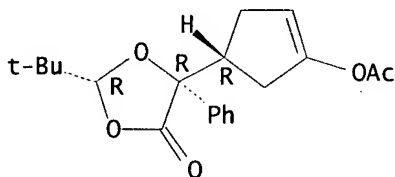
Absolute stereochemistry.



RN 389889-48-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(1R)-3-(acetyloxy)-3-cyclopenten-1-yl]-2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

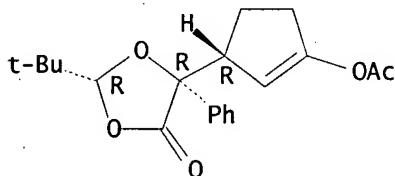
Absolute stereochemistry.



RN 389889-49-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(1R)-3-(acetyloxy)-2-cyclopenten-1-yl]-2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

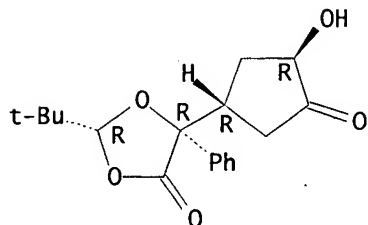
Absolute stereochemistry.



RN 389889-50-3 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-[(1R,3R)-3-hydroxy-4-oxocyclopentyl]-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

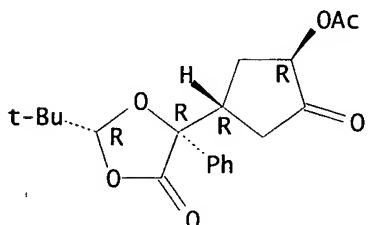
Absolute stereochemistry.



RN 389889-51-4 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(1R,3R)-3-(acetyloxy)-4-oxocyclopentyl]-2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:442484 HCAPLUS

DOCUMENT NUMBER: 133:222319

TITLE: Synthesis of (R)-4,4,4-trifluoro-2-mercaptoputyric acid

AUTHOR(S): Schedel, H.; Quaedflieg, P. J. L. M.; Broxterman, Q. B.; Bisson, W.; Duchateau, A. L. L.; Maes, I. C. H.; Herzsuh, R.; Burger, K.

CORPORATE SOURCE: Johannisallee 29, Institut für Organische Chemie, Universität Leipzig, Leipzig, 04103, Germany

SOURCE: Tetrahedron: Asymmetry (2000), 11(10), 2125-2131  
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:222319

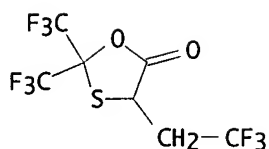
AB Syntheses of (R)-4,4,4-trifluoro-2-mercaptoputyric acid from (S)-malic acid via a Mitsunobu reaction and from (rac)-thiomalic acid on enzymic resolu., using Pseudomonas cepacia (Amano lipase PS), are described. A new method for direct detn. of ees for (R)- and (S)-4,4,4-trifluoro-2-mercaptoputyric acid derivs. by HPLC on a polysaccharide phase is disclosed.

IT 291772-68-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(alcoholysis of)

RN 291772-68-4 HCAPLUS

CN 1,3-Oxathiolan-5-one, 4-(2,2,2-trifluoroethyl)-2,2-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)



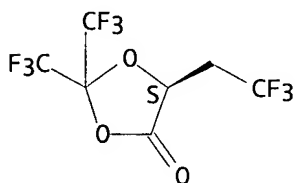
IT 291772-62-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
(methanolysis of)

RN 291772-62-8 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(2,2,2-trifluoroethyl)-2,2-bis(trifluoromethyl)-,  
(5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:83103 HCAPLUS

DOCUMENT NUMBER: 130:237395

TITLE: Regio- and enantioselectivity of the  
enzyme-catalyzed hydrolysis of citric acid  
derivativesAUTHOR(S): Chenevert, Robert; Ngatcha, Beatrice Tchedam; Rose,  
Yannick Stephane; Goupil, DanielCORPORATE SOURCE: Departement de chimie, Faculte des sciences et de  
genie, Universite Laval, QC, G1K 7P4, Can.SOURCE: Tetrahedron: Asymmetry (1998), 9(24), 4325-4329  
CODEN: TASYE3; ISSN: 0957-4166

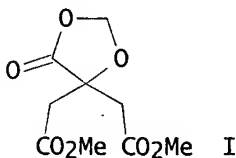
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:237395

GI

AB The hydrolysis of tri-Et citrate in the presence of three serine proteases  
(chymotrypsin, subtilisin BPN', subtilisin carlsberg) is highly  
regioselective and gives the sym. diester. Several lipases and proteases

have the complementary regioselectivity and give the chiral diester. Pig liver esterase, *Aspergillus niger* lipase and *Candida antarctica* lipase give the chiral (R)-diester with good regio- and enantioselectivity. The stereoselective hydrolysis of the meso citric deriv. I in the presence of *Candida antarctica* lipase gives the corresponding (R)-monoester.

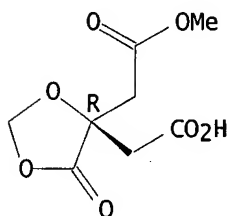
IT 199341-35-0P 221303-18-0P

RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(regio- and enantioselectivity of enzyme-catalyzed hydrolysis of citric acid derivs.)

RN 199341-35-0 HCAPLUS

CN 1,3-Dioxolane-4,4-diacetic acid, 5-oxo-, monomethyl ester, (4R)- (9CI)  
(CA INDEX NAME)

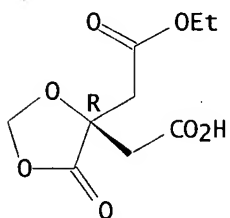
Absolute stereochemistry. Rotation (+).



RN 221303-18-0 HCAPLUS

CN 1,3-Dioxolane-4,4-diacetic acid, 5-oxo-, monoethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 9001-62-1, Lipase 9016-18-6, Esterase

RL: CAT (Catalyst use); USES (Uses)  
(regio- and enantioselectivity of enzyme-catalyzed hydrolysis of citric acid derivs.)

RN 9001-62-1 HCAPLUS

CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9016-18-6 HCAPLUS

CN Esterase, carboxyl (8CI, 9CI) (CA INDEX NAME)

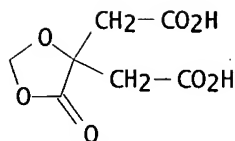
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 144-16-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(regio- and enantioselectivity of enzyme-catalyzed hydrolysis of citric acid derivs.)

RN 144-16-1 HCAPLUS

CN 1,3-Dioxolane-4,4-diacetic acid, 5-oxo- (9CI) (CA INDEX NAME)



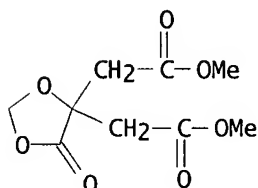
IT 77862-72-7P 112535-39-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(regio- and enantioselectivity of enzyme-catalyzed hydrolysis of citric acid derivs.)

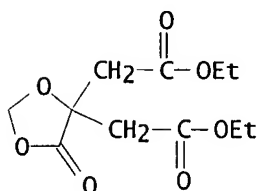
RN 77862-72-7 HCAPLUS

CN 1,3-Dioxolane-4,4-diacetic acid, 5-oxo-, dimethyl ester (9CI) (CA INDEX NAME)



RN 112535-39-4 HCAPLUS

CN 1,3-Dioxolane-4,4-diacetic acid, 5-oxo-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:539418 HCAPLUS

DOCUMENT NUMBER: 125:275318

TITLE: Lipase AKG mediated resolutions of .alpha.,.alpha.-disubstituted 1,2-diols in organic solvents; remarkably high regio- and enantioselectivity

AUTHOR(S): Hof, Robert P.; Kellogg, Richard M.  
CORPORATE SOURCE: Dep. Org. Mol. Inorg. Chem., Univ. Groningen, Groningen, 9747 AG, Neth.

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1996), (16), 2051-2060

CODEN: JCPRB4; ISSN: 0300-922X

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Diols, HOCH<sub>2</sub>CR(OH)Ph (I, R = Et, Pr, CH<sub>2</sub>Ph, 1-naphthylmethyl, etc.), which contain adjacent tertiary and primary hydroxy groups, can be selectively mono-acylated at the primary hydroxy group by many lipases in org. solvents. Since the reaction does not take place at the chiral tertiary center itself, obsd. enantioselectivities are usually low. Only the combination of one lipase, lipase AKG (Amano, Pseudomonas sp.), with selected substrates gives high enantioselectivities (E 20 to >200). Also, the solvent and acyl donor employed influences the outcome. On the basis of the results of lipase AKG towards substrates I, an active site model for this specific lipase has been developed which can account for the results obtained. Full exptl. details on the synthesis of diols I and enzymic prepn. of the acetates are given. Also, the abs. stereochem. of the enzymically prepd. diols I has been established by independent synthesis from (R)-mandelic acid.

IT 9001-62-1, Lipase  
 RL: CAT (Catalyst use); USES (Uses)  
 (prepn. and lipase-catalyzed resoln. of diols)

RN 9001-62-1 HCAPLUS

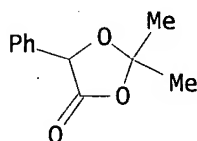
CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 6337-34-4 116907-30-3 182309-17-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. and lipase-catalyzed resoln. of diols)

RN 6337-34-4 HCAPLUS

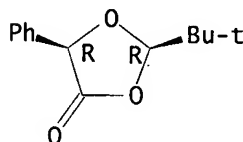
CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl- (8CI, 9CI) (CA INDEX NAME)



RN 116907-30-3 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-phenyl-, (2R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

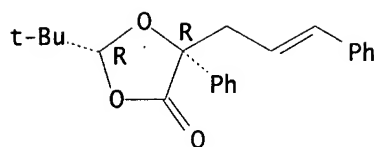


RN 182309-17-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 2-(1,1-dimethylethyl)-5-phenyl-5-(3-phenyl-2-propenyl)-, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.





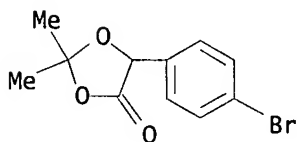
IT 42216-15-9P 129286-24-4P 136962-22-6P  
 136962-23-7P 136962-24-8P 179759-91-2P  
 182308-77-6P 182308-78-7P 182308-80-1P  
 182308-81-2P 182308-82-3P 182308-88-9P  
 182308-89-0P 182308-94-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(prepn. and lipase-catalyzed **resoln.** of diols)

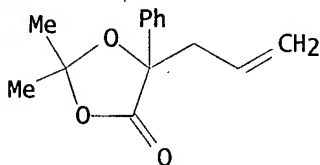
RN 42216-15-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-bromophenyl)-2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 129286-24-4 HCAPLUS

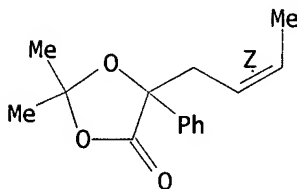
CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl-5-(2-propenyl)- (9CI) (CA INDEX NAME)



RN 136962-22-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(2-butenyl)-2,2-dimethyl-5-phenyl-, (Z)- (9CI) (CA INDEX NAME)

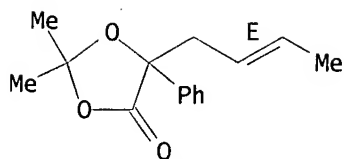
Double bond geometry as shown.



RN 136962-23-7 HCAPLUS

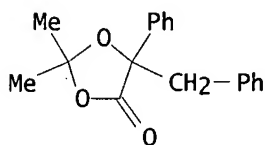
CN 1,3-Dioxolan-4-one, 5-(2-butenyl)-2,2-dimethyl-5-phenyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



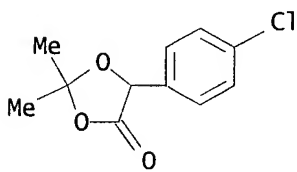
RN 136962-24-8 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



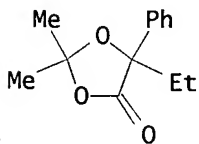
RN 179759-91-2 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-chlorophenyl)-2,2-dimethyl- (9CI) (CA INDEX NAME)



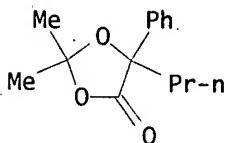
RN 182308-77-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-ethyl-2,2-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



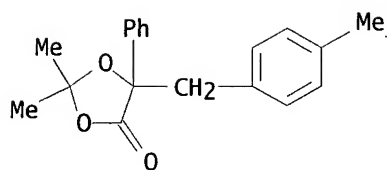
RN 182308-78-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl-5-propyl- (9CI) (CA INDEX NAME)

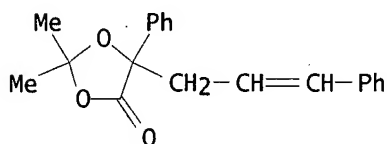


RN 182308-80-1 HCAPLUS

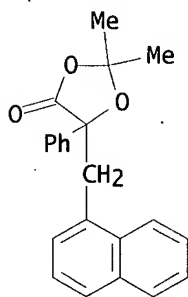
CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-[(4-methylphenyl)methyl]-5-phenyl- (9CI) (CA INDEX NAME)



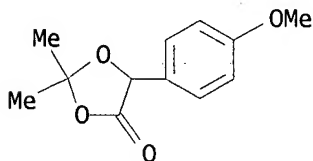
RN 182308-81-2 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl-5-(3-phenyl-2-propenyl)- (9CI)  
(CA INDEX NAME)

RN 182308-82-3 HCAPLUS

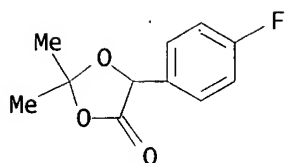
CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-(1-naphthalenylmethyl)-5-phenyl- (9CI)  
(CA INDEX NAME)

RN 182308-88-9 HCAPLUS

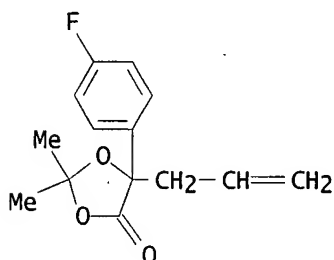
CN 1,3-Dioxolan-4-one, 5-(4-methoxyphenyl)-2,2-dimethyl- (9CI) (CA INDEX  
NAME)

RN 182308-89-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-fluorophenyl)-2,2-dimethyl- (9CI) (CA INDEX  
NAME)



RN 182308-94-7 HCAPLUS  
 CN 1,3-Dioxolan-4-one, 5-(4-fluorophenyl)-2,2-dimethyl-5-(2-propenyl)- (9CI)  
 (CA INDEX NAME)



L45 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1996:386456 HCAPLUS  
 DOCUMENT NUMBER: 125:167859  
 TITLE: Kinetic **resolution** of trans-2-(1-pyrazolyl)cyclohexan-1-ol catalyzed by **lipase** B from *Candida antarctica*  
 AUTHOR(S): Barz, M.; Herdtweck, E.; Thiel, W. R.  
 CORPORATE SOURCE: Anorganisch-chemisches Inst., Technische Univ. Muenchen, Garching, D-85747, Germany  
 SOURCE: Tetrahedron: Asymmetry (1996), 7(6), 1717-1722  
 CODEN: TASYE3; ISSN: 0957-4166  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The reaction of epoxycyclohexane with pyrazole gives trans-2-(1-pyrazolyl)cyclohexan-1-ol (rac-I) in high yields. Rac-I forms dimers in the solid state by linking one (1R,2R)- and one (1S,2S)-enantiomer via strong intermol. H-bonds. In the presence of the immobilized lipase B of *Candida antarctica* yeast, rac-I is acylated enantioselectively with isopropenylacetate acting as the acylating agent. Crystn. of the reaction mixt. gives enantiomerically pure (1S,2S)-I, which forms a helical structure in the solid state. The abs. configuration of this alc. was examd. by x-ray structure anal. of the esterification product with 5-oxo-(2R)-(trichloromethyl)-1,3-dioxolane-(4S)-acetylchloride.

IT **9001-62-1, Lipase**  
 RL: CAT (Catalyst use); USES (Uses)  
 (kinetic **resoln.** of pyrazolylcyclohexanol catalyzed by **lipase B**)

RN 9001-62-1 HCAPLUS  
 CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

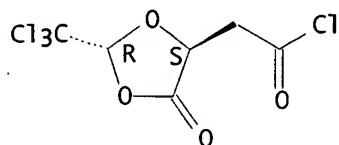
IT **173325-34-3**  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(kinetic **resoln.** of pyrazolylcyclohexanol catalyzed by  
lipase B)

RN 173325-34-3 HCAPLUS

CN 1,3-Dioxolane-4-acetyl chloride, 5-oxo-2-(trichloromethyl)-, (2R,4S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



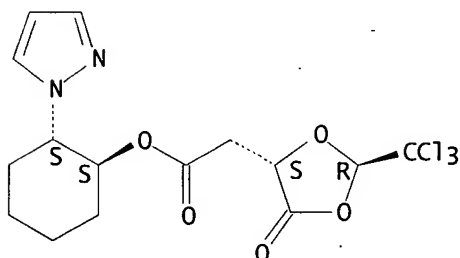
IT 180333-31-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(kinetic **resoln.** of pyrazolylcyclohexanol catalyzed by  
lipase B)

RN 180333-31-7 HCAPLUS

CN 1,3-Dioxolane-4-acetic acid, 5-oxo-2-(trichloromethyl)-,  
2-(1H-pyrazol-1-yl)cyclohexyl ester, [2R-[2.alpha.,4.beta.(1S\*,2S\*)]]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:259703 HCAPLUS

DOCUMENT NUMBER: 125:11273

TITLE: Synthesis and Lipase-Catalyzed  
**Resolution** of 5-(Hydroxymethyl)-1,3-dioxolan-4-  
ones: Masked Glycerol Analogs as Potential Building  
Blocks for Pharmaceuticals

AUTHOR(S): Hof, Robert P.; Kellogg, Richard M.

CORPORATE SOURCE: Department of Organic and Molecular Inorganic  
Chemistry, University of Groningen, Groningen, 9747  
AG, Neth.

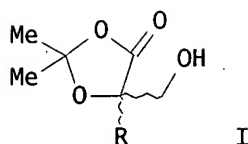
SOURCE: Journal of Organic Chemistry (1996), 61(10), 3423-7  
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB (Hydroxymethyl)-1,3-dioxolan-4-ones from mandelic and lactic acids and 1,5,5-trimethyl-3-phenyloxazolidin-2-one from mandelamide were .alpha.-alkylated using benzyl chloromethyl ether. Reductive debenzoylation of the products of alkylation unmasked the hydroxymethyl groups gave the corresponding glycerol analogs, e.g. I (R = Me, Ph). The compds. obtained in this fashion were subsequently subjected to lipase-catalyzed resoln. in org. media. Depending on the lipase and substrate employed, enantiomeric ratios up to E = 200 were obsd. The obtained optically pure compds. can be considered as masked 2-substituted glycerol equiv., which could be used for the prepn. of tertiary (aryloxy)propanolamines, compds. having potential .beta.-blocking activity.

IT 177089-32-6P 177089-33-7P 177089-34-8P  
177089-35-9P 177089-36-0P 177089-37-1P  
177089-38-2P 177089-39-3P 177089-40-6P  
177089-41-7P 177089-42-8P 177089-43-9P

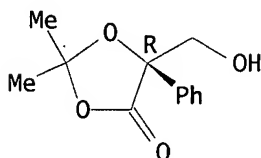
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and lipase-catalyzed resoln. of hydroxymethyldioxolanones as potential potential .beta.-blocking activity)

RN 177089-32-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2-dimethyl-5-phenyl-, (R)- (9CI)  
(CA INDEX NAME)

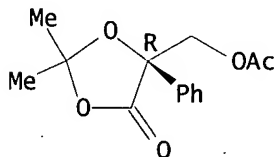
Absolute stereochemistry.



RN 177089-33-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-2,2-dimethyl-5-phenyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

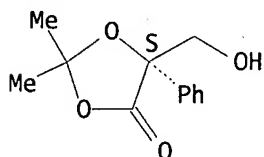


RN 177089-34-8 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2-dimethyl-5-phenyl-, (S)- (9CI)

(CA INDEX NAME)

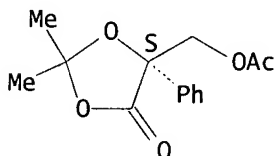
Absolute stereochemistry.



RN 177089-35-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-2,2-dimethyl-5-phenyl-, (S)-  
(9CI) (CA INDEX NAME)

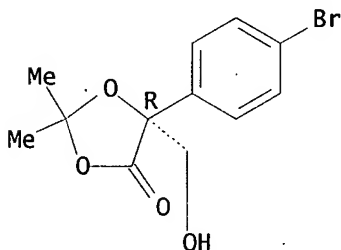
Absolute stereochemistry.



RN 177089-36-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-bromophenyl)-5-(hydroxymethyl)-2,2-dimethyl-,  
(R)- (9CI) (CA INDEX NAME)

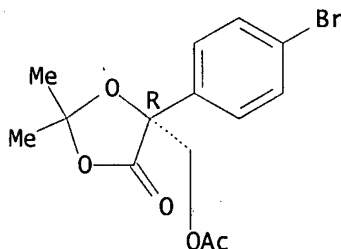
Absolute stereochemistry.



RN 177089-37-1 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-5-(4-bromophenyl)-2,2-dimethyl-,  
(R)- (9CI) (CA INDEX NAME)

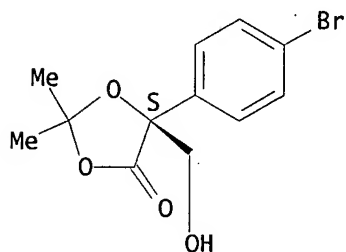
Absolute stereochemistry.



RN 177089-38-2 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-bromophenyl)-5-(hydroxymethyl)-2,2-dimethyl-,  
(S)- (9CI) (CA INDEX NAME)

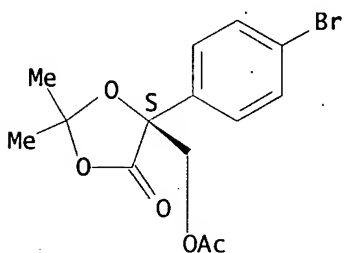
Absolute stereochemistry.



RN 177089-39-3 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-5-(4-bromophenyl)-2,2-dimethyl-,  
(S)- (9CI) (CA INDEX NAME)

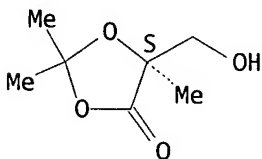
Absolute stereochemistry.



RN 177089-40-6 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2,5-trimethyl-, (S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

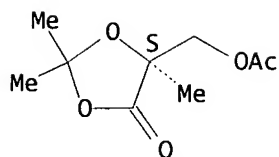


RN 177089-41-7 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-2,2,5-trimethyl-, (S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

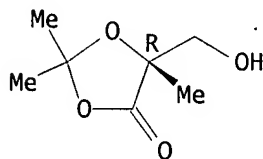




RN 177089-42-8 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2,5-trimethyl-, (R)- (9CI) (CA INDEX NAME)

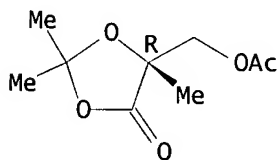
Absolute stereochemistry.



RN 177089-43-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-[(acetyloxy)methyl]-2,2,5-trimethyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



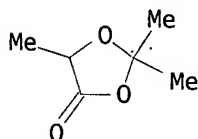
IT 4158-85-4 6337-34-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and lipase-catalyzed **resoln.** of hydroxymethyldioxolanones as potential potential .beta.-blocking activity)

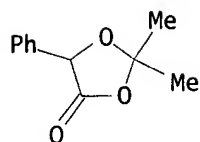
RN 4158-85-4 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2,5-trimethyl- (8CI, 9CI) (CA INDEX NAME)



RN 6337-34-4 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl- (8CI, 9CI) (CA INDEX NAME)



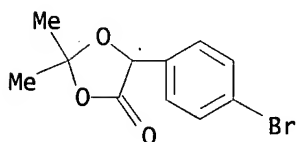
IT 42216-15-9P 81503-25-5P 81503-39-1P  
177089-27-9P 177089-28-0P 177089-30-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and lipase-catalyzed resolu. of hydroxymethyldioxolanones as potential potential .beta.-blocking activity)

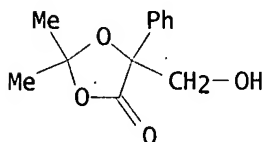
RN 42216-15-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-bromophenyl)-2,2-dimethyl- (9CI) (CA INDEX NAME)



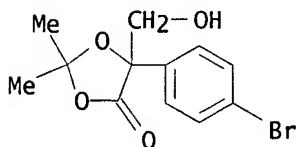
RN 81503-25-5 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



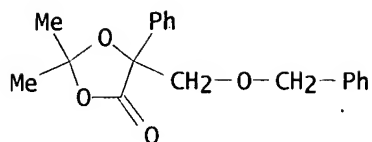
RN 81503-39-1 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(4-bromophenyl)-5-(hydroxymethyl)-2,2-dimethyl- (9CI) (CA INDEX NAME)



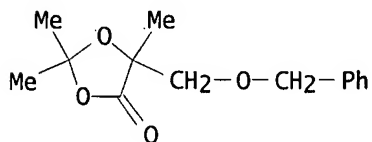
RN 177089-27-9 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2-dimethyl-5-phenyl-5-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)



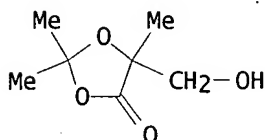
RN 177089-28-0 HCAPLUS

CN 1,3-Dioxolan-4-one, 2,2,5-trimethyl-5-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)



RN 177089-30-4 HCAPLUS

CN 1,3-Dioxolan-4-one, 5-(hydroxymethyl)-2,2,5-trimethyl- (9CI) (CA INDEX NAME)



L45 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:608463 HCAPLUS

DOCUMENT NUMBER: 115:208463

TITLE: Synthesis of BCH-189 and related compounds

INVENTOR(S): Liotta, Dennis C.; Choi, Woo Baeg

PATENT ASSIGNEE(S): Emory University, USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

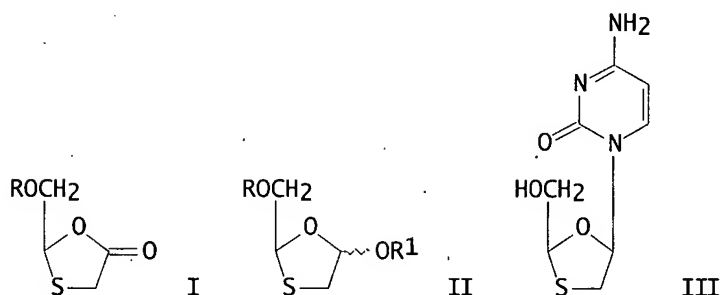
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

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WO 9111186	A1	19910808	WO 1991-US685	19910131
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RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5204466	A	19930420	US 1990-473318	19900201
CA 2075189	AA	19900802	CA 1991-2075189	19910131
AU 9173004	A1	19910821	AU 1991-73004	19910131
AU 658136	B2	19950406		
EP 513200	A1	19921119	EP 1991-904454	19910131
EP 513200	B1	19980909		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

HU 62566	A2	19930528	HU 1992-2496	19910131
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JP 07000618	B4	19950111		
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AT 170750	E	19980915	AT 1991-904454	19910131
EP 872237	A1	19981021	EP 1998-201737	19910131
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ES 2076130	T3	19990301	ES 1991-904454	19910131
JP 2001019690	A2	20010123	JP 2000-160358	19910131
JP 2001352997	A2	20011225	JP 2001-151617	19910131
JP 2002012591	A2	20020115	JP 2001-151618	19910131
FI 9203446	A	19920730	FI 1992-3446	19920730
NO 9203014	A	19920730	NO 1992-3014	19920730
US 5539116	A	19960723	US 1993-15992	19930210
US 5914400	A	19990622	US 1995-472345	19950607
AU 9540319	A1	19960426	AU 1995-40319	19951211
AU 698859	B2	19981112		
NO 9700385	A	19920730	NO 1997-385	19970129
NO 9700386	A	19920730	NO 1997-386	19970129
HK 1014664	A1	20000526	HK 1998-116019	19981228
US 6153751	A	20001128	US 1999-337910	19990622
AU 9944745	A1	19991111	AU 1999-44745	19990826
AU 715577	B3	20000203	AU 1999-59571	19991119
PRIORITY APPLN. INFO.:			US 1990-473318	A 19900201
			AU 1991-73004	A3 19910131
			EP 1991-904454	A3 19910131
			JP 1991-504897	A3 19910131
			WO 1991-US685	A 19910131
			US 1993-15992	A1 19930210
			US 1994-215498	B1 19940321
			US 1995-472345	A1 19950607

OTHER SOURCE(S): CASREACT 115:208463; MARPAT 115:208463  
GI



AB .beta.-Nucleosides are prepd. by reducing lactones I (R = protective group) followed by acylation, treating esters II (R<sub>1</sub> = acyl) with a silylated pyrimidine nucleic acid base in the presence of SnCl<sub>4</sub>, and deblocking. Thus, I (R = SiPh<sub>2</sub>CM<sub>3</sub>) was prepd. from allyl alc. via cyclization of HCOCH<sub>2</sub>OSiPh<sub>2</sub>CM<sub>3</sub> with HSCH<sub>2</sub>CO<sub>2</sub>H. Redn. of I (R = SiPh<sub>2</sub>CM<sub>3</sub>) and acetylation gave II (R = SiPh<sub>2</sub>CM<sub>3</sub>, R<sub>1</sub> = Ac). The latter compd. was treated with silylated cytosine and SnCl<sub>4</sub>, followed by deblocking to give BCH-189 (III) in 100% enantiomeric excess.

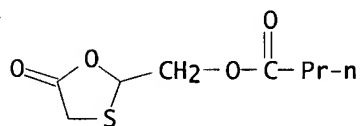
IT 136891-16-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)  
(prepn. and enzymic resoln. of)

RN 136891-16-2 HCAPLUS

CN Butanoic acid, (5-oxo-1,3-oxathiolan-2-yl)methyl ester (9CI) (CA INDEX NAME)



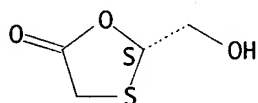
IT 136831-96-4P 137125-19-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and redn. of)

RN 136831-96-4 HCAPLUS

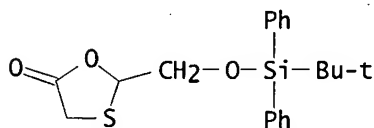
CN 1,3-Oxathiolan-5-one, 2-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 137125-19-0 HCAPLUS

CN 1,3-Oxathiolan-5-one, 2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-  
(9CI) (CA INDEX NAME)



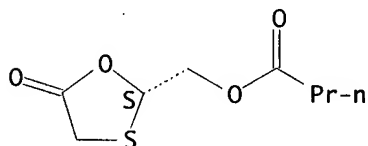
IT 136831-88-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 136831-88-4 HCAPLUS

CN Butanoic acid, (5-oxo-1,3-oxathiolan-2-yl)methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



# Cas react search

MARX 10/059,774

=> D QUE L44

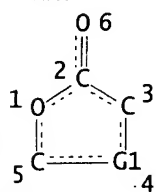
L23

L24

L38

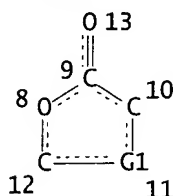
1 SEA FILE=REGISTRY ABB=ON PLU=ON LIPASE/CN  
2 SEA FILE=REGISTRY ABB=ON PLU=ON ESTERASE/CN  
STR

RRT



S @7

PRO



product

reactant

VAR G1=O/7

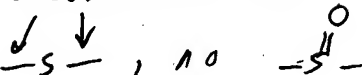
NODE ATTRIBUTES:

CONNECT IS E2 RC AT 7 - make the S an ether

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

2 connections



GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE

L40 153 SEA FILE=CASREACT SSS FUL L38 ( 1469 REACTIONS)

L41 2315 SEA FILE=CASREACT ABB=ON PLU=ON L23 OR LIPASE

L42 652 SEA FILE=CASREACT ABB=ON PLU=ON L24 OR ESTERASE

L43 9720 SEA FILE=CASREACT ABB=ON PLU=ON ?ENZYME?

L44 4 SEA FILE=CASREACT ABB=ON PLU=ON L40 AND (L41 OR L42 OR L43)

4 cites

=&gt; d ibib abs FCRDREF 1-4

L44 ANSWER 1 OF 4 CASREACT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:139499 CASREACT

TITLE: Method for the **enzymatic** preparation of

enantiomerically pure derivatives of

1,3-dioxolan-4-one and 1,3-oxathiolan-5-one

INVENTOR(S): Popp, Alfred; Stohrer, Juergen; Petersen, Hermann;

Gilch, Andrea; Rockinger-Mechlem, Jodoca

PATENT ASSIGNEE(S): Consortium Fuer Elektrochemische Industrie Gmbh,

Germany

SOURCE: Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

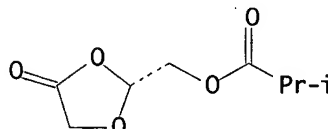
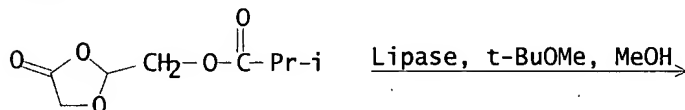
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1229127	A1	20020807	EP 2002-1124	20020124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
DE 10104231	A1	20020808	DE 2001-10104231	20010131
JP 2002281997	A2	20021002	JP 2002-22091	20020130
PRIORITY APPLN. INFO.:			DE 2001-10104231	20010131

OTHER SOURCE(S): MARPAT 137:139499

AB. A process is provided for the prodn. of enantiomerically pure derivs. of 1,3-dioxolan-4-one and 1,3-oxathiolan-5-one by an **enzyme** mediated kinetic resoln. of a racemate. When a racemic 1,3-dioxolan-4-one or 1,3-oxathiolan-5-one deriv. is mixed with a **lipase** or **esterase** in the presence of an oxygen contg. nucleophile, the dioxolane/ oxathiolane ring of one enantiomer is hydrolyzed at faster rate than the other enantiomer. Thus, 2-methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is mixed with Novozym 435 (a com. **lipase**) and methanol, (+)-(R)-2-Methylpropanoic acid(4-oxo-1,3-dioxolan-2-yl)methyl ester is produced with an enantiomeric excess > 98%.

RX(1) OF 7



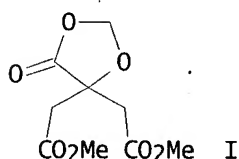
20%

REF: Eur. Pat. Appl., 1229127, 07 Aug 2002

NOTE: biotransformation, enzymic, novozym 435 used, batch process reaction, stereoselective

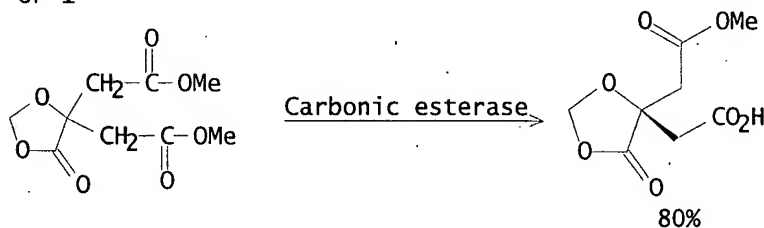
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 4 CASREACT COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 130:237395 CASREACT  
 TITLE: Regio- and enantioselectivity of the enzyme  
 -catalyzed hydrolysis of citric acid derivatives  
 AUTHOR(S): Chenevert, Robert; Ngatcha, Beatrice Tchedam; Rose,  
 Yannick Stephane; Goupil, Daniel  
 CORPORATE SOURCE: Departement de chimie, Faculte des sciences et de  
 genie, Universite Laval, QC, G1K 7P4, Can.  
 SOURCE: Tetrahedron: Asymmetry (1998), 9(24), 4325-4329  
 CODEN: TASYE3; ISSN: 0957-4166  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB The hydrolysis of tri-Et citrate in the presence of three serine proteases (chymotrypsin, subtilisin BPN', subtilisin carlsberg) is highly regioselective and gives the sym. diester. Several **lipases** and proteases have the complementary regioselectivity and give the chiral diester. Pig liver **esterase**, *Aspergillus niger* **lipase** and *Candida antarctica* **lipase** give the chiral (R)-diester with good regio- and enantioselectivity. The stereoselective hydrolysis of the meso citric deriv. I in the presence of *Candida antarctica* **lipase** gives the corresponding (R)-monoester.

RX(1) OF 1



REF: Tetrahedron: Asymmetry, 9(24), 4325-4329; 1998  
 NOTE: phosphate buffer

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 4 CASREACT COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 117:27001 CASREACT



TITLE: Synthesis, crystal structure, and some reactions of 2,3,4-tri-O-acetyl-.beta.-D-galactopyranurono-6,1-lactone

AUTHOR(S): Vogel, Christian; Liebelt, Bernd; Steffan, Wolfram; Kristen, Helmut

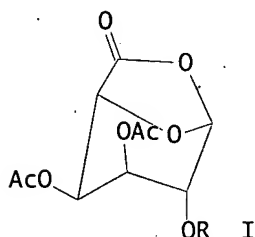
CORPORATE SOURCE: Fachbereich Chem., Univ. Rostock, Rostock, O-2500, Germany

SOURCE: Journal of Carbohydrate Chemistry (1992), 11(3), 287-303  
CODEN: JCACDM; ISSN: 0732-8303

DOCUMENT TYPE: Journal

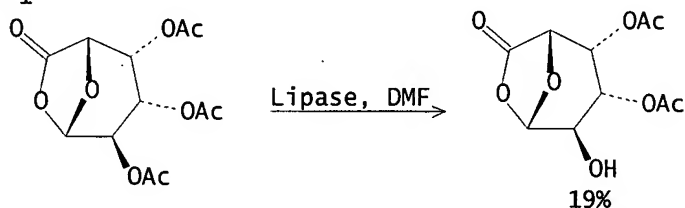
LANGUAGE: English

GI



AB D-Gluco-, D-galacto-, And D-manno-6,1-lactones of uronic acid were synthesized. A new synthetic approach based on the photobromination, hydrolysis, and oxidn. of the corresponding 1,6-anhydro sugars, is reported. Conformational studies and crystal structure of title compd. (I; R = Ac) (II), were undertaken. Regioselective deacetylation catalyzed by wheat germ lipase of II gave I (R = H).

RX(1) OF 1



REF: Journal of Carbohydrate Chemistry, 11(3), 287-303; 1992  
NOTE: enzymic, buffer soln.

L44 ANSWER 4 OF 4 CASREACT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 113:211510 CASREACT

TITLE: Pig-liver-esterase-catalyzed hydrolyses of racemic .alpha.-substituted .alpha.-hydroxy esters

AUTHOR(S): Moorlag, Henk; Kellogg, Richard M.; Kloosterman, Marcel; Kaptein, Bernard; Kamphuis, Johan; Schoemaker, Hans E.

CORPORATE SOURCE: Bio-Org. Chem. Sect., DSM Res., Geleen, 6160 MD, Neth.

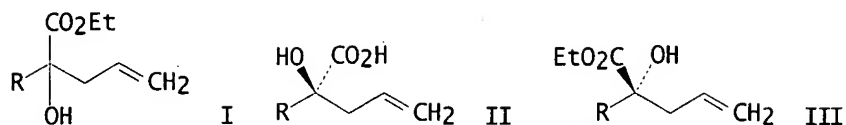
SOURCE: Journal of Organic Chemistry (1990), 55(23), 5878-81

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

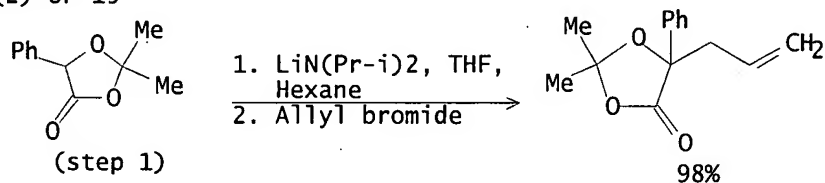
LANGUAGE:  
GI

English



AB Pig liver **esterase** catalyzed hydrolyses of some  $\alpha$ -substituted  $\alpha$ -hydroxy esters I (R = Ph, Me) give product acids II and recovered esters III in 9-94% enantiomeric excess. The obsd. enantiomeric selectivity could be rationalized using a recently proposed active site model, which proved to be of predictive value.

RX(2) OF 15



REF: Journal of Organic Chemistry, 55(23), 5878-81; 1990

# term search in WPIX (Derwent)

MARX 10/059,774

=> D QUE L50

L46	3603	SEA FILE=WPIX ABB=ON	PLU=ON	?OXATHIOLAN? OR ?DIOXOLAN?
L47	28	SEA FILE=WPIX ABB=ON	PLU=ON	L46 AND (RESOLV? OR RESOLUTION)
L48	107	SEA FILE=WPIX ABB=ON	PLU=ON	L46 AND ENANTIO?
L50	19	SEA FILE=WPIX ABB=ON	PLU=ON	(L47 OR L48) AND (LIPASE OR ESTERASE OR ?ENZYM?)

19 cites

=&gt; d ibib abs L50 1-19

L50 ANSWER 1 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-601293 [65] WPIX  
 DOC. NO. CPI: C2002-170101  
 TITLE: Preparation of **enantiomerically** pure 1,3-  
**dioxolan-4-one** or 1,3-**oxathiolan-5-one**  
 derivative, for use e.g. as antiviral agent intermediate,  
 by **enantio-selective enzymatic**  
 cleavage of unwanted isomer in racemate.  
 DERWENT CLASS: B03 D16  
 INVENTOR(S): GILCH, A; PETERSEN, H; POPP, A; ROCKINGER-MECHLEM, J;  
 STOHRER, J  
 PATENT ASSIGNEE(S): (CONE) CONSORTIUM ELEKTROCHEM IND GMBH  
 COUNTRY COUNT: 28  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1229127	A1	20020807	(200265)*	GE	14
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CA 2369718	A1	20020731	(200265)	EN	
DE 10104231	A1	20020808	(200265)		
JP 2002281997	A	20021002	(200279)		10

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1229127	A1	EP 2002-1124	20020124
CA 2369718	A1	CA 2002-2369718	20020130
DE 10104231	A1	DE 2001-10104231	20010131
JP 2002281997	A	JP 2002-22091	20020130

PRIORITY APPLN. INFO: DE 2001-10104231 20010131

AN 2002-601293 [65] WPIX

AB EP 1229127 A UPAB: 20021010

NOVELTY - Preparation of **enantiomerically** pure 1,3-  
**dioxolan-4-one** or 1,3-**oxathiolan-5-one** derivatives (I)  
 involves (i) contacting a mixture of the **enantiomers** of (I) with  
 a hydrolytic **enzyme** and a nucleophile, so that the ring of one  
**enantiomer** of (I) is cleaved by the **enzyme**; and (ii)  
 isolating the non-cleaved **enantiomer** of (I).

USE - **Enantiomerically** pure (I) are especially useful as  
 intermediates for antiviral agents, particularly nucleoside analogs such  
 as **dioxolane-T** or **coviracil**. More generally  
**enantiomerically** pure products are useful as starting materials or  
 intermediates for agrochemicals and pharmaceuticals.

ADVANTAGE - **Enantiomers** of (I) are obtained inexpensively,  
 with high **enantioselectivity** and **regioselectivity**. The products  
 formed in cleavage of the unwanted **enantiomer** of (I) can be  
 recovered and reacted to give further racemic (I) starting material, thus  
 reducing costs and consumption of chemicals.  
 Dwg.0/0

L50 ANSWER 2 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-370027 [40] WPIX

CROSS REFERENCE: 2002-423615 [45]  
 DOC. NO. CPI: C2002-104756  
 TITLE: **Enantioselective lipase** and  
 burkholderia cocovenenans sy-01 strain producing the  
 same.  
 DERWENT CLASS: B03 D16  
 INVENTOR(S): BAE, H G; HAN, Y S; JUNG, C S; KIM, S I; LEE, B S; PARK,  
 H I; PARK, J G; SHIN, P G; YOON, M Y  
 PATENT ASSIGNEE(S): (HANA-N) HANALL PHARM CO LTD; (KOAD) KOREA ADV INST SCI &  
 TECHNOLOGY; (KYUN-N) KYUNG DONG PHARMA CO LTD  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 2001109632	A	20011212	(200240)*		1

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 2001109632	A	KR 2000-29739	20000531

PRIORITY APPLN. INFO: KR 2000-29739 20000531

AN 2002-370027 [40] WPIX

CR 2002-423615 [45]

AB KR2001109632 A UPAB: 20021018

NOVELTY - Provided are **enantioselective lipase** and  
 Burkholderia cocovenenans SY-01 strain producing the same, where the  
**lipase enantioselectively** decomposes ester bonding of a  
 racemic compound, cis-2-(bromethyl)-2-(2,4-dichloro phenyl)-1,3-  
**dioxolane-4-methyl acetate**, as an intermediate of intraconazole.

DETAILED DESCRIPTION - **Enantioselective lipase** is  
 produced from Burkholderia cocovenenans SY-01 strain (KFCC-11111), has  
 39KD of MW, and shows activity at 45-50 deg. C, pH7.0-9.0. A single isomer  
 is isolated from cis-2-(bromethyl)-2-(2,4-dichloro phenyl)-13-  
**dioxolane-4-methyl acetate** using the culture of Burkholderia  
 cocovenenans SY-01 strain.  
 Dwg.1/10

L50. ANSWER 3 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-141512 [19] WPIX

CROSS REFERENCE: 1993-038535 [05]

DOC. NO. CPI: C2002-043758

TITLE: (-)-4-amino-5-fluoro-1-(2-hydroxymethyl)-1,3-  
**oxathiolan-5-yl)-(1H)-pyrimidin-2-one** or its  
 salt, useful for treating viral infections.

DERWENT CLASS: A89 B03 D16

INVENTOR(S): DIONNE, G

PATENT ASSIGNEE(S): (BIOC-N) BIOCHEM PHARMA INC

COUNTRY COUNT: 17

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1155695	A1	20011121	(200219)*	EN	15
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1155695	A1 Div ex	EP 1992-307051	19920803
		EP 2001-119636	19920803

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1155695	A1 Div ex	EP 526253

PRIORITY APPLN. INFO: GB 1991-16601 19910801

AN 2002-141512 [19] WPIX

CR 1993-038535 [05]

AB EP 1155695 A UPAB: 20020321

NOVELTY - (-)-4-Amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one (A) or its salt, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the preparation of (A) involving separating (-)-**enantiomer** from a mixture also containing the (+)-**enantiomer**.

ACTIVITY - Antiviral; Anti-HIV; Hepatotropic; Antiinflammatory; Nootropic; Cytostatic; Antimicrobial. Antiviral activity of (A) in C8166 cells (human T-lymphoblastoid cell line, infected with HIV-1 strain RF) was determined by inhibition of syncytium formation according to Tochikura et al virology, 164, 652-546. (A) was administered in an amount of 0.14 mu g/ml. The 50% antiviral activity (%) involving the inhibition of syncytium formation was 0.0018.

MECHANISM OF ACTION - Inhibitor of retrovirus replication including human retrovirus such as human immuno deficiency virus.

USE - In the manufacture of a medicament for the treatment of viral, HIV or hepatitis B infection (claimed); in the treatment of AIDS related conditions such as AIDS related complex, progressive generalized lymphadenopathy, AIDS-related neurological conditions e.g. dementia or tropical paraparesis, anti HIV antibody positive and HIV-positive conditions, Kaposi's sarcoma, thrombocytopenia purpura and other infections including Pneumocystis carinii.

ADVANTAGE - (-)-**enantiomer** of the compound is much more active than (+)-**enantiomer**. The (-)-**enantiomer** shows low toxicity.  
Dwg.0/0

L50 ANSWER 4 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2001-589752 [66] WPIX

DOC. NO. CPI: C2001-174835

TITLE: New **esterase enzymes**, useful for **enantioselective** synthesis of e.g. alcohols, acids and lactones by hydrolysis of substrates.

DERWENT CLASS: B05 D16

INVENTOR(S): ALLEN, L; BRIKUM, I; FREIJE, D; MORIS-VARAS, F

PATENT ASSIGNEE(S): (THER-N) THERMOGEN INC

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001060986	A2	20010823	(200166)*	EN	37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM					

MARX 10/059,774

DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC  
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE  
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
AU 2001038407 A 20010827 (200176)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001060986	A2	WO 2001-US5059	20010216
AU 2001038407	A	AU 2001-38407	20010216

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001038407	A Based on	WO 200160986

PRIORITY APPLN. INFO: US 2000-183634P 20000218; US 2000-182863P  
20000216; US 2000-183104P 20000217

AN 2001-589752 [66] WPIX

AB WO 200160986 A UPAB: 20011113

NOVELTY - **Esterase** (I) having the biochemical fingerprint (BF)  
of one of NE01-NE22, as defined by

(i) reaction and **enantioselectivity** profiles to 26  
specified substrates and

(ii) the pNP (p-nitrophenyl) propionate profile.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for  
selective hydrolysis of substrates using (I).

USE - (I) are useful (i) for **enantioselective** hydrolysis of  
(thio)esters, e.g. for **resolving** racemates; (ii) for synthesis  
of optically active acids, alcohols, esters, lactones or detergents and  
(iii) in ripening of cheese.

Dwg.0/4

L50 ANSWER 5 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2000-339331 [29] WPIX

DOC. NO. CPI: C2000-102912

TITLE: **Enantioselective** conversion of  
**enantiomeric** mixtures of hydrophobic esters using  
a biphasic solvent system and biocatalyst, useful for  
preparing antiviral compounds.

DERWENT CLASS: A96 B03 D16

INVENTOR(S): WANG, Y F; YAO, Y

PATENT ASSIGNEE(S): (ALTU-N) ALTUS BIOLOGICS INC

COUNTRY COUNT: 91

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2000022157	A1	20000420	(200029)*	EN	62
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RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES  
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL  
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000011044 A 20000501 (200036)

EP 1119635 A1 20010801 (200144) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI  
 BR 9914375 A 20011120 (200202)  
 CN 1329671 A 20020102 (200227)  
 KR 2001099679 A 20011109 (200229)  
 JP 2002527073 W 20020827 (200271)

65

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000022157	A1	WO 1999-US23405	19991008
AU 2000011044	A	AU 2000-11044	19991008
EP 1119635	A1	EP 1999-954779	19991008
		WO 1999-US23405	19991008
BR 9914375	A	BR 1999-14375	19991008
		WO 1999-US23405	19991008
CN 1329671	A	CN 1999-811893	19991008
KR 2001099679	A	KR 2001-704430	20010407
JP 2002527073	W	WO 1999-US23405	19991008
		JP 2000-576047	19991008

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000011044	A Based on	WO 200022157
EP 1119635	A1 Based on	WO 200022157
BR 9914375	A Based on	WO 200022157
JP 2002527073	W Based on	WO 200022157

PRIORITY APPLN. INFO: US 1998-103804P 19981009

AN 2000-339331 [29] WPIX

AB WO 200022157 A UPAB: 20000617

NOVELTY - A chiral, non-racemic ester is prepared from an **enantiomeric** mixture of the hydrophobic ester using a hydrolase **enzyme** in a biphasic solvent system.

DETAILED DESCRIPTION - Preparation of a chiral, nonracemic ester comprises:

(a) dispersing an **enantiomeric** mixture of a hydrophobic ester at 1-25% (w/v of the non-homogeneous system) in an organic solvent system; and

(b) contacting the organic mixture from (a) with an aqueous solvent system, providing **resolution** of the mixture to produce a chiral nonracemic ester and a non-racemic alcohol.

The hydrolase **enzyme** is dispersed in the organic component, aqueous component or the non-homogeneous system.

An INDEPENDENT CLAIM is included for a non-homogeneous system for producing a chiral, non-racemic hydrophobic ester comprising:

- (i) a hydrolase **enzyme**;
- (ii) a hydrophobic ester substrate;
- (iii) an organic component; and
- (iv) an aqueous component.

USE - For preparation of antiviral compounds, e.g. 2 hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane.

ADVANTAGE - The use of a non-homogeneous system having incompletely water miscible organic co-solvents provides improved solvation for hydrophobic esters compared to systems using water miscible organic solvents.

Dwg.0/0



L50 ANSWER 6 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 2000-195020 [17] WPIX  
 DOC. NO. CPI: C2000-060394  
 TITLE: Preparation of 5-oxo-7H-pyrido-(2,1-b)(1,3)thiazepine-7-carboxylic acid derivative used for treating cardiovascular diseases involves using new dioxalane intermediates.  
 DERWENT CLASS: B02 B03  
 INVENTOR(S): DILLON, J L; GODFREY, J D; JASS, P A; KOTNIS, A S; KRONENTHAL, D R; POWERS, G L; RACHA, S; RAMIG, K; SCHWINDEN, M D; SOUNDARARAJAN, N; SRIVASTAVA, S K; VENIT, J J  
 PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO  
 COUNTRY COUNT: 86  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000003981	A2	20000127	(200017)*	EN	34
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SISK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9948528	A	20000207	(200029)		
US 6166227	A	20001226	(200103)		
US 6248882	B1	20010619	(200137)		
EP 1121351	A2	20010808	(200146)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6329542	B1	20011211	(200204)		
KR 2001071895	A	20010731	(200208)		
MX 2001000252	A1	20010601	(200235)		
HU 2001005151	A2	20020429	(200238)		
JP 2002520389	W	20020709	(200259)		39
AU 753189	B	20021010	(200279)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000003981	A2	WO 1999-US14957	19990701
AU 9948528	A	AU 1999-48528	19990701
US 6166227	A Provisional	US 1998-92944P	19980715
		US 1999-349867	19990708
US 6248882	B1 Provisional	US 1998-92944P	19980715
		US 2000-689209	20001012
EP 1121351	A2	EP 1999-932163	19990701
		WO 1999-US14957	19990701
US 6329542	B1 Provisional	US 1998-92944P	19980715
	Div ex	US 1999-349867	19990708
		US 2000-689215	20001012
KR 2001071895	A	KR 2001-700563	20010113
MX 2001000252	A1	MX 2001-252	20010109
HU 2001005151	A2	WO 1999-US14957	19990701
		HU 2001-5151	19990701
JP 2002520389	W	WO 1999-US14957	19990701
		JP 2000-560090	19990701
AU 753189	B	AU 1999-48528	19990701

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9948528	A Based on	WO 200003981
EP 1121351	A2 Based on	WO 200003981
US 6329542	B1 Div ex	US 6166227
HU 2001005151	A2 Based on	WO 200003981
JP 2002520389	W Based on	WO 200003981
AU 753189	B Previous Publ. Based on	AU 9948528 WO 200003981

PRIORITY APPLN. INFO: US 1998-92944P 19980715; US 1999-349867  
 19990708; US 2000-689209 20001012; US  
 2000-689215 20001012

AN 2000-195020 [17] WPIX

AB WO 200003981 A UPAB: 20020730

NOVELTY - Preparation of (4S-(4 alpha (R asterisk ),7 alpha ,10 alpha beta ))-octahydro-4-((2-mercapto-1-oxo-3-phenylpropyl)amino)-5-oxo-7H-pyrido-(2,1-b)(1,3)thiazepine-7-carboxylic acid (X) involves using new dioxolane intermediates (III) and (IV).

DETAILED DESCRIPTION - Preparation of (4S-(4 alpha (R asterisk ),7 alpha ,10 alpha beta ))-octahydro-4-((2-mercapto-1-oxo-3-phenylpropyl)amino)-5-oxo-7H-pyrido-(2,1-b)(1,3)thiazepine-7-carboxylic acid (X) comprises:

(1) reacting a glycinamide compound of formula (I) with a dioxolane compound of formula (II);

(2) treating the obtained dioxolane compound of formula (III) with water under reflux;

(3) treating the obtained dioxolane pentanoic acid compound of formula (IV) to exchange the dioxolane acetal with a dimethoxy acetal and convert the carboxylic acid to the methyl ester;

(4) coupling the obtained (S)-2-amino-6,6-dimethoxyhexanoic acid, methyl ester (XI) with an N-protected amino acid of formula (V);

(5) removing the P2 mercapto group from the obtained dipeptide of formula (VI) followed by acid catalyzed cyclization;

(6) removing the P1 amino protecting group from the obtained lactam compound of formula (VII) followed by coupling with an acylmercaptoalkanoic acid compound of formula (VIII) and

(7) treating the obtained compound of formula (IX) to remove R6CO and convert the methyl ester to the carboxylic acid and produce (X).

L = a leaving group;

P1 = amino protecting group;

P2 = mercapto protecting group;

R6 = methyl or phenyl.

INDEPENDENT CLAIMS are included for the following:

(A) new compounds (III) and (IV);

(B) preparation of (III) and (IV) as in (1) and (2) above;

(C) preparation of (S)-2-amino-6,6-dimethoxyhexanoic acid, methyl ester as in (3) above or by steps (1)-(3) per se;

(D) preparation of (X) by steps (3)-(7) per se and

(E) storage stable salts of (S)-2-amino-6,6-dimethoxyhexanoic acid, methyl ester.

ACTIVITY - Cardiant.

MECHANISM OF ACTION - Neutral endopeptidase inhibitor; angiotensin converting enzyme inhibitor.

USE - (I) (omapatrilat) is used for treating cardiovascular diseases e.g. hypertension and congestive heart failure.

ADVANTAGE - Different stages of the process may be carried out at different manufacturing facilities to give increased flexibility.

Oxidation reaction and optical **resolution** are eliminated.  
Dwg.0/0

L50 ANSWER 7 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 2000-182440 [16] WPIX  
 DOC. NO. CPI: C2000-057086  
 TITLE: Stereoselective reductive amination of ketoacid  
 derivatives, to give alpha-aminoalkanoic acid derivatives  
 useful in synthesis of cardiovascular agents, using amino  
 acid dehydrogenase and co-factor.  
 DERWENT CLASS: B03 B05 D16  
 INVENTOR(S): DONOVAN, M J; GOLDBERG, S; HANSON, R; JASS, P A; LI, W;  
 PATEL, R; RAMIG, K; SZARKA, L J; VENIT, J J; HANSON, R L;  
 PATEL, R N  
 PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO; (HANS-I) HANSON R L;  
 (JASS-I) JASS P A; (LIWW-I) LI W; (PATE-I) PATEL R;  
 (RAMI-I) RAMIG K; (VENI-I) VENIT J J  
 COUNTRY COUNT: 84  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000004179	A1	20000127	(200016)*	EN	64
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9949735	A	20000207	(200029)		
US 6140088	A	20001031	(200057)		
EP 1097236	A1	20010509	(200128)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
KR 2001071908	A	20010731	(200208)		
US 2002049342	A1	20020425	(200233)		
MX 2001000512	A1	20010701	(200236)		
HU 2001005062	A2	20020429	(200238)		
JP 2002520065	W	20020709	(200259)		80
US 6468781	B1	20021022	(200277)#		
US 6486331	B2	20021126	(200281)		
AU 755530	B	20021212	(200305)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000004179	A1	WO 1999-US15343	19990707
AU 9949735	A	AU 1999-49735	19990707
US 6140088	A Provisional	US 1998-92935P	19980715
		US 1999-350428	19990708
EP 1097236	A1	EP 1999-933744	19990707
		WO 1999-US15343	19990707
KR 2001071908	A	KR 2001-700599	20010115
US 2002049342	A1 Provisional	US 1998-92935P	19980715
	Div ex	US 1999-350428	19990708
	Div ex	US 2000-510925	20000222
		US 2001-848464	20010503
MX 2001000512	A1	MX 2001-512	20010115
HU 2001005062	A2	WO 1999-US15343	19990707

MARX 10/059,774

JP 2002520065 W		HU 2001-5062	19990707
		WO 1999-US15343	19990707
		JP 2000-560276	19990707
US 6468781	B1 Div ex	US 1999-350428	19990708
		US 2000-510925	20000222
US 6486331	B2 Provisional	US 1998-92935P	19980715
	Div ex	US 1999-350428	19990708
	Div ex	US 2000-510925	20000222
		US 2001-848464	20010503
AU 755530	B	AU 1999-49735	19990707

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9949735	A Based on	WO 200004179
EP 1097236	A1 Based on	WO 200004179
US 2002049342	A1 Div ex	US 6140088
HU 2001005062	A2 Based on	WO 200004179
JP 2002520065 W	Based on	WO 200004179
US 6468781	B1 Div ex	US 6140088
US 6486331	B2 Div ex	US 6140088
AU 755530	B Previous Publ.	AU 9949735
	Based on	WO 200004179

PRIORITY APPLN. INFO: US 1998-92935P 19980715; US 1999-350428  
19990708; US 2000-510925 20000222; US  
2001-848464 20010503

AN 2000-182440 [16] WPIX

AB WO 200004179 A UPAB: 20000330

NOVELTY - Production of alpha -aminoalkanoic acid derivatives (I) comprises reductive amination of corresponding keto compound (II) in presence of ammonia, an amino acid dehydrogenase (AADH) and co-factor.

DETAILED DESCRIPTION - Production of alpha -aminoalkanoic acid derivatives of formula (I) comprises reductive amination of corresponding keto compound of formula (II) using an amino acid dehydrogenase in presence of ammonia and co-factor.

R1 = H, 1-18C alkyl or monovalent cation;

R2 = 1,3-dioxolan-2-yl (a); -CH(OR3)2 (b) or 4,4-di-R4-1,2-dioxan-2-yl (c);

R3 = 1-18C alkyl;

R4 = H or R3.

INDEPENDENT CLAIMS are also included for the following:

(1) engineered yeast host cells that produce both phenylalanine dehydrogenase (PDH) and formate dehydrogenase (FDH) comprising: (a) a recombinant nucleic acid encoding PDH and optionally an endogenous nucleic acid encoding PDH; and (b) a recombinant and/or endogenous nucleic acid encoding FDH;

(2) engineered bacterial host cells containing recombinant nucleic acid that expresses a phenylalanine dehydrogenase and endogenous nucleic acid that expresses a formate dehydrogenase;

*Pichia pastoris* ATCC 74408 and ATCC 74433 and *E. coli* ATCC 98374; and

(3) compounds (II).

USE - (I) are intermediates in synthesis of compounds, described in US5508272, that inhibit angiotensin-converting enzyme and neutral endopeptidase, useful for treating cardiovascular disease.

ADVANTAGE - The reductive amination is **enantioselective** (giving the (S)-**enantiomer** with optical purity over 99%); requires only one step and provides high conversion of (II) and yields of (I) over 80 (preferably 99) %.

Dwg.0/6

L50 ANSWER 8 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 1996-133434 [14] WPIX  
 DOC. NO. CPI: C1996-041262  
 TITLE: Optically active 1,2-di ol prepn. - by reacting  
 enantiomeric dioxolanone mixt. with pig  
 pancreatic lipase for selective hydrolysis.  
 DERWENT CLASS: B05 D16 E19  
 PATENT ASSIGNEE(S): (CHCC) CHISSO CORP  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 08023997	A	19960130	(199614)*		11

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 08023997	A	JP 1994-186406	19940714

PRIORITY APPLN. INFO: JP 1994-186406 19940714

AN 1996-133434 [14] WPIX

AB JP 08023997 A UPAB: 19960405

Prepn. of an optically active 1,2-diol comprises reacting a pig pancreatic lipase (or mixt. contg. pig pancreatic lipase) which can selectively hydrolyse the carbonate bond of 1 enantiomer in a mixt. of the cyclic carbonate of formula (I), with the enantiomer mixt. to form an optically active 1,2-diol of formula (II) or (III) and an optically active carbonate of the formula (IV) or (V).

The 1,2-diol is sepd. from the carbonate and the carbonate is hydrolysed in the presence of an alkali to prepare (II) or (III). Z = Me, O, S, NH, N(CH(CH<sub>3</sub>)<sub>2</sub>) or a gp. of formula (i), (ii), (iii), or (iv).

USE - The method can be used to prepare non-cyclic optically active (S) and (R)-1,2-diols in with a wide range of carbon numbers.

Dwg.0/0

L50 ANSWER 9 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 1995-045617 [07] WPIX  
 DOC. NO. CPI: C1995-020514  
 TITLE: New hydroxy phosphinyl leucyl tryptophan derivs - are  
 proendothelin convertase inhibitors useful for treating  
 e.g. ischaemia, asthma etc..  
 DERWENT CLASS: B02  
 INVENTOR(S): DE, NANTEUIL G; REMOND, G; VERBEUREN, T  
 PATENT ASSIGNEE(S): (ADIR) ADIR & CIE; (ADIR) ADIR  
 COUNTRY COUNT: 22  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2707089	A1	19950106	(199507)*		19
AU 9466025	A	19950112	(199509)		
EP 639586	A1	19950222	(199512)	FR	13
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
CA 2127067	A	19941231	(199513)	FR	
JP 07224091	A	19950822	(199542)		9

MARX 10/059,774

ZA 9404727	A	19950927 (199544)	19
US 5481030	A	19960102 (199607)	7
NZ 260873	A	19960126 (199610)	
NZ 270956	A	19960126 (199610)	
US 5591728	A	19970107 (199708)	6
US 5608045	A	19970304 (199715)	6
AU 677654	B	19970501 (199726)	
JP 2653976	B2	19970917 (199742)	9
CA 2127067	C	20001226 (200104)	FR
EP 639586	B1	20010321 (200117)	FR

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE  
DE 69426908 E 20010426 (200130)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2707089	A1	FR 1993-7927	19930630
AU 9466025	A	AU 1994-66025	19940628
EP 639586	A1	EP 1994-401268	19940608
CA 2127067	A	CA 1994-2127067	19940629
JP 07224091	A	JP 1994-147687	19940629
ZA 9404727	A	ZA 1994-4727	19940630
US 5481030	A	US 1994-267971	19940629
NZ 260873	A	NZ 1994-260873	19940629
NZ 270956	A	NZ 1994-270956	19940629
US 5591728	A Div ex	US 1994-267971	19940629
		US 1995-497811	19950703
US 5608045	A Div ex	US 1994-267971	19940629
		US 1995-497812	19950703
AU 677654	B	AU 1994-66025	19940628
JP 2653976	B2	JP 1994-147687	19940629
CA 2127067	C	CA 1994-2127067	19940629
EP 639586	B1	EP 1994-401268	19940608
DE 69426908	E	DE 1994-626908	19940608
		EP 1994-401268	19940608

FILING DETAILS:

PATENT NO	KIND	PATENT NO
NZ 270956	A Div ex	NZ 260873
US 5591728	A Div ex	US 5481030
US 5608045	A Div ex	US 5481030
AU 677654	B Previous Publ.	AU 9466025
JP 2653976	B2 Previous Publ.	JP 07224091
DE 69426908	E Based on	EP 639586

PRIORITY APPLN. INFO: FR 1993-7927 19930630

AN 1995-045617 [07] WPIX

AB FR 2707089 A UPAB: 19950602

Amino acid phosphonic acid derivs. of formula (I), their enantiomers, diastereoisomers, epimers and salts are new. R1 = OH, 1-6C alkoxy or amino opt. substd. by 1 - 2 1-6C alkyl; R2 = 1-6C alkyl opt. substd. by phenyl or 3-7C cycloalkyl; X1, X2 = -NH-, -O-, or -S-, R3 = H, 1-6C alkyl or phenyl; R4 = 1-6C alkyl (substd. by one or more OH, benzyloxy, benzyloxy carbonyl amino, amino, mono- or di-(1-6C)alkyl amino or acetoxy), 3-7C cycloalkyl (opt. substd. by one or more OH, benzyloxy or acetoxy) or R4-X2-PO(OR3)- = a gp. of formula (a); n = 0 - 1; R5 = OH or -CH2OH.

USE - (I) are useful as endothelin converting enzyme (proendothelin convertase) inhibitors and are useful in the treatment of ischaemia, hypertension, angina, myocardial infarction, renal insufficiency, shock, diabetes, hypercholesterolaemia, Raynauds disease, cardiac insufficiency, hypoxic pulmonary vasoconstriction, asthma, atherosclerosis, and arthritis.

Dwg.0/0

ABEQ US 5481030 A UPAB: 19960222

Cpd of formula (I) its **enantiomers**, diastereoisomers and epimers as well as its addition salts with a pharmaceutically-acceptable acid or base.

R1 = hydroxyl, (C1-C6) alkoxy or amino (opt. substd. with (C1-C6) alkyl); R2 = (C1-C6) alkyl, opt. substd. phenyl or (C3-C7) cycloalkyl; X1 = -NH-; X2 = O; R3 = hydrogen, (C1-C6) alkyl or phenyl; R4 = (C1-C6) alkyl opt. substd. with hydroxyl, benzyloxy, benzyloxy carbonylamino, amino, (C1-C6) mono- or dialkylamino, acetoxy, or 2,2-dimethyl-1,3-dioxolan-4-yl; R5 = 3-indolylmethyl, naphthylmethyl, (C1-C6) alkyl, phenyl, or benzyl.

Dwg.0/0

ABEQ US 5591728 A UPAB: 19970220

A method for treating a mammal afflicted with a condition requiring an endothelin convertase inhibitor comprising the step of administering to the mammal an amount of a compound selected from those of formula (R4)-(X2)-P(=O)(OR3)X1-CH(R2)C(O)-NH-CH(R5)(-C(O)(R1)) (I) in which:

R1 represents hydroxyl, linear or branched (C1-C6) alkoxy, or amino which is unsubstituted or substituted with 1 or 2 linear or branched (C1-C6) alkyl,

R2 represents linear or branched (C1-C6) alkyl, unsubstituted or substituted with phenyl or C3-C7) cycloalkyl,

X1 represents -NH-,

X2 represents -O-,

R3 represents hydrogen, linear or branched (C1-C6) alkyl, or phenyl,

R4 represents linear or branched (C1-C6) alkyl which is substituted with one or more hydroxyl, benzyloxy, benzyloxycarbonylamino, amino linear or branched (C1-C6) mono- or dialkylamino, acetoxy, or 2,2-dimethyl-1,3-dioxolan-4-yl, such groups being identical or different,

R5 represent 3-indolylmethyl, naphthylmethyl, linear or branched (C1-C6) alkyl, phenyl, or benzyl,

its **enantiomers**, diastereoisomers and epimers as well as its addition salts with a pharmaceutically-acceptable acid or base, which is effective for alleviation of said condition.

Dwg.0/0

ABEQ US 5608045 A UPAB: 19970410

A process for preparing phosphoramidon disodium salt (N-[alpha-(S)-(rhamnopyranosyloxy)hydroxyphosphinyl]-(S)Leu-(S)Trp-OH disodium salt) wherein the starting material is one equivalent of rhamnosetriacetate, which is reacted in a pot reaction with one equivalent of phenyl dichlorophosphate in the presence of two equivalents of triethylamine and with (S)Leu-(S)Trp-OEt in a suitable solvent, whereafter the product is separated and saponified with an ethanolic base in the cold and the ethanol evaporated to leave an oil.

Dwg.0/0

L50 ANSWER 10 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1993-368810 [46] WPIX

DOC. NO. CPI: C1993-163746

TITLE: **Enantiomeric** pure beta-adrenergic blockers  
prepn. for antihypertensives - using **enantiomeric**  
enriched glycerol carbonate prep. by esterifying

racemate with **enzyme** for selectivity.  
 DERWENT CLASS: B03 D16  
 INVENTOR(S): CASSEL, J M; OLIVERO, A G; POULSEN, J R  
 PATENT ASSIGNEE(S): (COGN-N) COGNIS INC  
 COUNTRY COUNT: 31  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9322451	A1	19931111	(199346)*	EN	23
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CZ FI HU JP KR NO NZ PL RU SK UA					
AU 9339781	A	19931129	(199411)		
US 5326885	A	19940705	(199426)		6

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9322451	A1	WO 1993-US3514	19930419
AU 9339781	A	AU 1993-39781	19930419
US 5326885	A Cont of	US 1992-877556	19920501
		US 1993-140799	19931021

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9339781	A Based on	WO 9322451

PRIORITY APPLN. INFO: US 1992-877556 19920501

AN 1993-368810 [46] WPIX

AB WO 9322451 A UPAB: 19940103

Prepn. comprises esterifying the racemate under the influence of a hydrolytic **enzyme** which selectively esterifies the S isomer of the racemate.

Also new is the prepn. of an **enantiomerically** pure beta-adrenergic blocker of formula (III) comprising reacting an **enantiomerically** enriched glycerol carbonate of formula (I) with a reactant of formula ArOM1 (IV) to give an intermediate of formula (II) and reacting (II) with an amine of formula NR1R2R3 in the presence of a halide salt of formula M2X. In the formulae, L = leaving gp. of alkyl sulphonate, aryl sulphonate, I, Br or Cl; Ar = opt. substd. 6-20C aryl; M1 = Li, Na or K; R1, R2 = alkyl, aryl or benzyl; X = F, Cl, Br or I; and M2 = Li, Na, K, Mg, NMe4, N(Bu)4 or P(Bu)4.

USE/ADVANTAGE - (III) are beta-adrenergic blockers e.g. S-atenolol, S-toliprolol, S-bunolol, S-peributolol, S-propanolol, S-timolol and other aryloxy- propanolamine antihypertensive agents. The prodn. prepares **enantiomerically** pure pharmaceutical prods., esp. pref. by avoiding the potential for an inactive **enantiomer** to interfere with the activity of the therapeutically effective isomer or to produce adverse side effects.

Dwg.0/0

ABEQ US 5326885 A UPAB: 19940817

(S)-2-oxo-4-(sulphonyloxymethyl) -1,3-dioxolanes of formula (I) contain **enzymically** enriched (R)-glycerol 1,3-carbonate units. In (I), R is opt. cyclopentyl- or cyclohexyl-substd. 1-20C alkyl or 3-6C cycloalkyl, or opt. halogen-, NO2- or alkyl-substd. 6-10C aryl.

USE/ADVANTAGE - The prods. are intermediates for the prepn. of (R)-glycerol carbonate and **enantiomerically** pure beta-adrenergic



blockers. Enzymes are available for the specific hydrolysis or esterification of (S)-glycerol carbonate, facilitating the prepn. of corresp. (R)-enantiomers.  
Dwg.0/0

L50 ANSWER 11 OF 19 WPIX (C) 2003 THOMSON DERWENT  
ACCESSION NUMBER: 1992-316114 [38] WPIX  
CROSS REFERENCE: 1991-252418 [34]; 1992-316105 [38]; 1998-085641 [06]  
DOC. NO. CPI: C1992-140435  
TITLE: New antiviral 5-(5-fluoro-cytosin-1-yl)-1,3-oxathiolane nucleoside(s) - for treating HIV, HBV and SIV infections, and related conditions e.g. ARG, PGL, Kaposi's sarcoma, neuropathy etc..  
DERWENT CLASS: B02 B03 D16  
INVENTOR(S): CHOI, W; LIOTTA, D C; SCHINAZI, R F  
PATENT ASSIGNEE(S): (UYEM-N) UNIV EMORY  
COUNTRY COUNT: 40  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9214743	A2	19920903	(199238)*	EN	72
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL OA SE					
W: AU BB BG BR CA FI HU JP KP KR LK MG MW NO PL RO RU SD					
AU 9215617	A	19920915	(199251)		
CN 1065065	A	19921007	(199324)		
PT 100151	A	19930531	(199325)		
CZ 9200497	A3	19930317	(199329)		
FI 9303684	A	19930906	(199347)		
NO 9302980	A	19930820	(199347)		
EP 575482	A1	19931229	(199401)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
BR 9205661	A	19940524	(199424)		
HU 65548	T	19940628	(199429)		
JP 06508605	W	19940929	(199443)		
WO 9214743	A3	19921029	(199511)		
AU 665187	B	19951221	(199607)		
AU 9537943	A	19960314	(199618)		
NZ 241625	A	19960326	(199618)		
NZ 250842	A	19960326	(199618)		
AU 679649	B	19970703	(199735)		
CN 1127301	A	19960724	(199749)		
JP 10147586	A	19980602	(199832)		32
AU 9880773	A	19981015	(199902)		
CN 1203232	A	19981230	(199920)		
JP 2901160	B2	19990607	(199928)		31
US 5914331	A	19990622	(199931)		
EP 984013	A2	20000308	(200017)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
IL 100965	A	19991231	(200018)		
KR 172590	B1	19990201	(200039)		
US 6114343	A	20000905	(200044)		
AU 2000066703	A	20010111	(200108)#		
NO 312399	B1	20020506	(200238)		
JP 3292830	B2	20020617	(200242)		28

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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MARX 10/059,774

WO 9214743	A2	WO 1992-US1339	19920220
AU 9215617	A	AU 1992-15617	19920220
		WO 1992-US1339	19920220
CN 1065065	A	CN 1992-101981	19920222
PT 100151	A	PT 1992-100151	19920221
CZ 9200497	A3	CS 1992-497	19920220
FI 9303684	A	WO 1992-US1339	19920220
		FI 1993-3684	19930820
NO 9302980	A	WO 1992-US1339	19920220
		NO 1993-2980	19930820
EP 575482	A1	EP 1992-908027	19920220
		WO 1992-US1339	19920220
BR 9205661	A	BR 1992-5661	19920220
		WO 1992-US1339	19920220
HU 65548	T	WO 1992-US1339	19920220
		HU 1993-2377	19920220
JP 06508605	W	JP 1992-507549	19920220
		WO 1992-US1339	19920220
AU 665187	B	AU 1992-15617	19920220
AU 9537943	A Div ex	AU 1992-15617	19920220
		AU 1995-37943	19951120
NZ 241625	A	NZ 1992-241625	19920217
NZ 250842	A	NZ 1992-250842	19920217
AU 679649	B Div ex	AU 1992-15617	19920220
		AU 1995-37943	19951120
CN 1127301	A Div ex	CN 1992-101981	19920222
		CN 1995-109814	19920222
JP 10147586	A Div ex	JP 1992-507549	19920220
		JP 1997-340469	19920220
AU 9880773	A Div ex	AU 1995-37943	19951120
		AU 1998-80773	19980817
CN 1203232	A Div ex	CN 1992-101981	19920222
		CN 1998-108905	19920222
JP 2901160	B2	JP 1992-507549	19920220
		WO 1992-US1339	19920220
US 5914331	A CIP of CIP of CIP of Cont of	US 1990-473318	19900201
		US 1991-659760	19910222
		US 1991-736089	19910726
		US 1992-831153	19920212
		US 1995-488097	19950607
EP 984013	A2 Div ex	EP 1992-908027	19920220
		EP 1999-203367	19920220
IL 100965	A	IL 1992-100965	19920217
KR 172590	B1	WO 1992-US1339	19920220
		KR 1993-702516	19930821
US 6114343	A CIP of CIP of CIP of CIP of Cont of Cont of Cont of	US 1990-473318	19900201
		US 1991-659760	19910222
		US 1991-736089	19910726
		US 1991-776072	19911011
		US 1992-831153	19920212
		US 1992-846303	19920305
		US 1995-451392	19950526
		US 1995-482875	19950607
AU 2000066703	A Div ex	AU 1998-80773	19980817
		AU 2000-66703	20001024
NO 312399	B1	WO 1992-US1339	19920220
		NO 1993-2980	19930820
JP 3292830	B2 Div ex	JP 1992-507549	19920220
		JP 1997-340469	19920220

## FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9215617	A	Based on	WO 9214743
EP 575482	A1	Based on	WO 9214743
BR 9205661	A	Based on	WO 9214743
HU 65548	T	Based on	WO 9214743
JP 06508605	W	Based on	WO 9214743
AU 665187	B	Previous Publ. Based on	AU 9215617 WO 9214743
NZ 250842	A	Div ex	NZ 241625
AU 679649	B	Previous Publ.	AU 9537943
JP 2901160	B2	Previous Publ. Based on	JP 06508605 WO 9214743
US 5914331	A	CIP of CIP of	US 5204466 US 5210085
EP 984013	A2	Div ex	EP 575482
US 6114343	A	CIP of CIP of	US 5204466 US 5210085
NO 312399	B1	Previous Publ.	NO 9302980
JP 3292830	B2	Previous Publ.	JP 10147586

PRIORITY APPLN. INFO: US 1992-831153 19920212; US 1991-659760  
 19910222; US 1991-736089 19910726; US  
 1990-473318 19900201; US 1995-488097  
 19950607; US 1991-776072 19911011; US  
 1992-846303 19920305; US 1995-451392  
 19950526; US 1995-482875 19950607; AU  
 2000-66703 20001024

AN 1992-316114 [38] WPIX

CR 1991-252418 [34]; 1992-316105 [38]; 1998-085641 [06]

AB WO 9214743 A UPAB: 20020704

beta-2-Hydroxymethyl -5-(5-fluorocytosin-1-yl)-1,3-oxathiolane  
 (FTC) as (I)-D,L, (-)-L, or (+)-D isomers, their derivs. all of formula  
 (I) or their salts, are new.

In (I) R1, R2 independently = alkyl, carboxylic ester in which the  
 non-carbonyl portion is straight, branched or cyclic alkyl, alkoxyalkyl,  
 aralkyl, aryloxyalkyl, aryl including phenyl opt. substd. with halo, 1-4C  
 alkyl, or 1-4C alkoxy, sulphonate ester, alkyl or aralkyl sulphonyl,  
 mono-m di- or tri-phosphate ester, or amino acid ester; and one of R1, R2  
 can be H.

Also claimed is a method for the **resolution** of nucleoside  
**enantiomers**, comprising exposure of the racemate to an  
**enzyme** that pref. catalyses a reaction in one of the  
**enantiomers**.

USE/ADVANTAGE - FTC shows surprisingly high activity against HIV with  
 very low toxicity. It competitively inhibits HIV-1 reverse transcriptase  
 with a K1 of 0.2 micromolar, using a poly(I) oligo (dC) template primer.  
 It is non-toxic to peripheral bone marrow cells at upto 50 micromolar, and  
 other cell lines of 200 micromolar.  
 Dwg.0/12

L50 ANSWER 12 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1992-316105 [38] WPIX

CROSS REFERENCE: 1991-252418 [34]; 1992-316114 [38]; 1998-085641 [08]

DOC. NO. CPI: C1992-140426

TITLE: 1,3-Diox lane nucleoside analogues prodn.,  
 useful as antiviral agents - from protected  
 2-hydroxymethyl -4-acyloxy-1,3-dioxolane and

protected purine or pyrimidine base using titanium catalyst.

DERWENT CLASS: B02 B03  
 INVENTOR(S): CHOI, W; LIOTTA, D C; SCHINAZI, R F; CHENG, Y  
 PATENT ASSIGNEE(S): (UYEM-N) UNIV EMORY; (UYA) UNIV YALE  
 COUNTRY COUNT: 21  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9214729	A1	19920903	(199238)*	EN	40
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE					
W: AU CA JP US					
AU 9214372	A	19920915	(199251)		
US 5210085	A	19930511	(199320)		24
ZA 9201251	A	19931027	(199348)		79
US 5276151	A	19940104	(199402)		10
US 5728575	A	19980317	(199818)		19
US 5814639	A	19980929	(199846)		
US 5827727	A	19981027	(199850)		19
US 5852027	A	19981222	(199907)		
US 5892025	A	19990406	(199921)		
IL 100965	A	19991231	(200018)		
US 6069252	A	20000530	(200033)		
KR 172590	B1	19990201	(200039)		
US 6346627	B1	20020212	(200219)		
US 2002143194	A1	20021003	(200267)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9214729	A1	WO 1992-US1393	19920221
AU 9214372	A	AU 1992-14372	19920221
		WO 1992-US1393	19920221
US 5210085	A CIP of	US 1990-473318	19900201
		US 1991-659760	19910222
ZA 9201251	A	ZA 1992-1251	19920220
US 5276151	A CIP of	US 1990-473318	19900201
	Cont of	US 1991-659760	19910222
	Cont of	US 1991-736089	19910726
		US 1991-803028	19911206
US 5728575	A CIP of	US 1990-473318	19900201
	CIP of	US 1991-659760	19910222
	Cont of	US 1991-736089	19910726
	Cont of	US 1993-92248	19930715
	Cont of	US 1995-402730	19950313
		US 1995-485318	19950607
US 5814639	A CIP of	US 1990-473318	19900201
	Div ex	US 1991-659760	19910222
		US 1993-17820	19930216
US 5827727	A CIP of	US 1990-473318	19900201
	CIP of	US 1991-659760	19910222
	Cont of	US 1991-736089	19910726
	Cont of	US 1993-92248	19930715
	Cont of	US 1995-402730	19950313
		US 1995-483653	19950607
US 5852027	A CIP of	US 1991-659760	19910222
	CIP of	US 1991-736089	19910726
	CIP of	US 1991-803028	19911206

MARX 10/059,774

			WO 1992-US1393	19920221
			US 1993-150012	19931109
US 5892025	A	CIP of	US 1990-473318	19900201
		CIP of	US 1991-659760	19910222
		Cont of	US 1991-736089	19910726
		Cont of	US 1993-92248	19930715
		Cont of	US 1995-402730	19950313
		Div ex	US 1995-483653	19950607
			US 1998-115780	19980714
IL 100965	A		IL 1992-100965	19920217
US 6069252	A	CIP of	US 1990-473318	19900201
		CIP of	US 1991-659760	19910222
		Cont of	US 1991-736089	19910726
		Cont of	US 1993-92248	19930715
		Cont of	US 1995-402730	19950313
			US 1995-474406	19950607
KR 172590	B1		WO 1992-US1339	19920220
			KR 1993-702516	19930821
US 6346627	B1	CIP of	US 1990-473318	19900201
		CIP of	US 1991-659760	19910222
		Cont of	US 1991-736089	19910726
		Cont of	US 1993-92248	19930715
		Cont of	US 1995-402730	19950313
			US 1995-482233	19950607
US 2002143194	A1	CIP of	US 1990-473318	19900201
		CIP of	US 1991-659760	19910222
		Cont of	US 1991-736089	19910726
		Cont of	US 1993-92248	19930715
		Cont of	US 1995-402730	19950313
		Cont of	US 1995-482233	19950607
			US 2002-73734	20020211

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9214372	A	Based on	WO 9214729
US 5728575	A	CIP of	US 5204466
		CIP of	US 5210085
US 5814639	A	CIP of	US 5204466
		Div ex	US 5210085
US 5827727	A	CIP of	US 5204466
		CIP of	US 5210085
US 5852027	A	CIP of	US 5210085
		CIP of	US 5276151
		Based on	WO 9214729
US 5892025	A	CIP of	US 5204466
		CIP of	US 5210085
		Div ex	US 5827727
US 6069252	A	CIP of	US 5204466
		CIP of	US 5210085
US 6346627	B1	CIP of	US 5204466
		CIP of	US 5210085
US 2002143194	A1	CIP of	US 5204466
		CIP of	US 5210085
		Cont of	US 6346627

PRIORITY APPLN. INFO: US 1991-803028 19911206; US 1991-659760  
 19910222; US 1991-736089 19910726; US  
 1990-473318 19900201; US 1993-92248

19930715; US 1995-402730 19950313; US  
 1995-485318 19950607; US 1993-17820  
 19930216; US 1995-483653 19950607; US  
 1993-150012 19931109; US 1998-115780  
 19980714; US 1992-831153 19920212; US  
 1995-474406 19950607; US 1995-482233  
 19950607; US 2002-73734 20020211

AN 1992-316105 [38] WPIX

CR 1991-252418 [34]; 1992-316114 [38]; 1998-085641 [08]

AB WO 9214729 A UPAB: 20021018

2'-Deoxy-5-fluoro -3'-oxacytidine (FDOC) and its (+) and (-) **enantiomers** are new.

Prodn. of 1,3-dioxolane nucleosides (I) is effected by reacting a 2-(protected hydroxymethyl) -4-acyloxy-1,3-dioxolane (II) with a protected purine or pyrimidine base (III) in the presence of a Ti catalyst of formula  $Ti(X)_n(Y)_4-n$  (IV)  $n = 2-4$ ;  $X = Cl, Br$  or  $I$ ;  $Y =$  alkoxy, aryloxy,  $NH_2$ , mono- or dialkylamino, mono- or diarylamino alkylarylamino, or  $Y+Y$  is a divalent gp. bonded to Ti through an alkoxy O atom and an amino N atom).

Optical **resolution** of racemic cpds. (I) is effected by treatment with an **enzyme** that preferentially catalyses a reaction in one of the **enantiomers**.

USE/ADVANTAGE - Cpds. (I), including FDOC, are antiviral agents esp. useful for treating HIV infections. Process (B) provides high beta-stereoselectivity at the  $C1'$  position.

Dwg.0/2

ABEQ US 5210085 A UPAB: 19931113

Treating HIV in humans comprises admin., of a beta isomer of a 2'-deoxy-5-fluoro-3'-thiacytidine of formula (I) where Y is H, opt. substd. alkyl, cycloalkyl or acyl; and R is H, OH, oxyacylormono-, di or triphosphate. (I) is pref. 4-N-acetyl-2'-deoxy-5-fluoro-3'-thia-cytidine; 4-N-acetyl-5'-butyryl-2'-deoxy-5-fluoro-3'-thiacytidine or 5'-butyryl-2'-deoxy-5-fluoro-3'-thiacytidine.

USE/ADVANTAGE - (I) are non toxic.

0/0

Dwg.0/0

ABEQ ZA 9201251 A UPAB: 19940120

Method comprises administering an effective amount of 2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane of formula (I), a pharmaceutically acceptable derivative thereof, including a 5' or  $N4$  alkylated or acylated derivative, or a pharmaceutically acceptable salt thereof, in a pharmaceutically acceptable carrier.

A process for the **resolution** of a racemic mixture of nucleoside **enantiomers** is also disclosed that includes the step of exposing the racemic mixture to an **enzyme** that preferentially catalyses a reaction in one of the **enantiomers**.

USE - For treatment of HIV and HBV infection in humans.

ABEQ US 5276151 A UPAB: 19940223

Prepn. of 1,3-dioxolane nucleosides comprises reaction of a 2-O-protected-5-O-acyl-1,3-dioxolane with a purine or pyrimidine having protected NH and OH gps. in the presence of a Ti halide catalyst of formula  $RiX_nY_m$ , where n is 2-4, m is 4-n, X is Cl, Br or I, and Y is alkaloxy or opt. alkyl- and/or aryl- mono- or di-substd.  $NH_2$ . Most of the prod. has a beta-structure at the  $C-1'$ -position of the 1,3-dioxolane ring. Typical prod. is 2-hydroxymethyl-5-(thymidine-1-yl or 5-fluorocytosine-1-yl) -1,3-dioxolane.

USE - The prods. are potential therapeutics for HIV infection (AIDS).

Dwg.0/2

ABEQ US 5728575 A UPAB: 19980507

2'-Deoxy-5-fluoro -3'-oxacytidine (FDOC) and its (+) and (-)

**enantiomers** are new.

Prodn. of 1,3-dioxolane nucleosides (I) is effected by reacting a 2-(protected hydroxymethyl) -4-acyloxy-1,3-dioxolane (II) with a protected purine or pyrimidine base (III) in the presence of a Ti catalyst of formula  $Ti(X)_n(Y)_{4-n}$  (IV)  $n = 2-4$ ;  $X = Cl, Br$  or  $I$ ;  $Y =$  alkoxy, aryloxy,  $NH_2$ , mono- or dialkylamino, mono- or diarylamino alkylaryl amino, or  $Y+Y$  is a divalent gp. bonded to Ti through an alkoxy O atom and an amino N atom).

Optical **resolution** of racemic cpds. (I) is effected by treatment with an **enzyme** that preferentially catalyses a reaction in one of the **enantiomers**.

USE/ADVANTAGE - Cpds. (I), including FDOC, are antiviral agents esp. useful for treating HIV infections. Process (B) provides high beta-stereoselectivity at the  $C1'$  position.

Dwg.0/8

L50 ANSWER 13 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 1991-353701 [48] WPIX  
 DOC. NO. CPI: C1991-152542  
 TITLE: (-)-Cis-4-amino-1-(2-hydroxymethyl-1,3-oxathiolanyl)-1H-pyrimidinone - useful in treating viral infections, e.g. HIV has lower cytotoxicity than (plus)-**enantiomer**.  
 DERWENT CLASS: B03  
 INVENTOR(S): COATES, J A V; MUTTON, I M; PENN, C R; STORER, R; WILLIAMSON, C; COATES, J; MUTTON, I; PENN, C; COATES, J A  
 PATENT ASSIGNEE(S): (BIOC-N) BIOCHEM PHARMA INC; (IAFB-N) IAF BIOCHEM INT INC; (IAFB-N) IAF BIO CHEM INT INC; (SHIL-N) SHILY BIOLOGICAL CHEM CO LTD; (IAFB-N) IAF BIOCHEM INT  
 COUNTRY COUNT: 39  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9117159	A	19911114	(199148)*		
RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE					
W: AU BG CA FI HU JP KR LK NO PL RO SU US					
AU 9177719	A	19911127	(199210)		
PT 97520	A	19920131	(199210)		
FI 9106165	A	19911230	(199213)		
ZA 9103293	A	19920226	(199214)		34
NO 9200018	A	19920102	(199219)		
CS 9101251	A2	19920115	(199233)		
CN 1058214	A	19920129	(199240)		
JP 05501117	W	19930304	(199314)		14
HU 64335	T	19931228	(199405)		
NZ 238017	A	19940627	(199426)		
AU 651345	B	19940721	(199432)		
EP 625150	A1	19941123	(199445)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
FI 9504183	A	19950906	(199548)		
IL 98025	A	19961016	(199648)		
NO 180377	B	19961230	(199707)		
CN 1108655	A	19950920	(199733)		
RO 112616	B1	19971128	(199819)		
SG 46383	A1	19980220	(199821)		
RU 2099338	C1	19971220	(199832)		18
KR 9607532	B1	19960605	(199919)		
JP 11080153	A	19990326	(199923)		15
JP 2927546	B2	19990728	(199935)		16

JP 2000128787 A 20000509 (200032) 15  
 TW 366346 A 19990811 (200032)  
 JP 3062475 B2 20000710 (200037) 15  
 EP 1062950 A2 20001227 (200102) EN  
 R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE  
 MX 193792 A 19991022 (200107)  
 US 6180639 B1 20010130 (200108)  
 CA 2059263 C 20010410 (200124) EN  
 CA 2337748 A1 19911114 (200132) EN  
 CZ 288499 B6 20010613 (200138)  
 CN 1326743 A 20011219 (200226)  
 US 2003004175 A1 20030102 (200305)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
ZA 9103293	A	ZA 1991-3293	19910430
NO 9200018	A	WO 1991-GB706	19910502
		NO 1992-18	19920102
CS 9101251	A2	CS 1991-1251	19910430
CN 1058214	A	CN 1991-102778	19910430
JP 05501117	W	JP 1991-508513	19910502
		WO 1991-GB706	19910502
HU 64335	T	WO 1991-GB706	19910502
		HU 1992-302	19910502
NZ 238017	A	NZ 1991-238017	19910501
AU 651345	B	AU 1991-77719	19910502
EP 625150	A1	EP 1991-920963	19910502
		WO 1991-GB706	19910502
FI 9504183	A	WO 1991-GB706	19910502
	Div ex	FI 1991-6165	19911230
		FI 1995-4183	19950906
IL 98025	A	IL 1991-98025	19910502
NO 180377	B	WO 1991-GB706	19910502
		NO 1992-18	19920102
CN 1108655	A	CN 1991-102778	19910430
	Div ex	CN 1994-109429	19910430
RO 112616	B1	RO 1991-149033	19910502
		WO 1991-GB706	19910502
SG 46383	A1	SG 1996-4002	19910502
RU 2099338	C1	WO 1991-GB706	19910502
		SU 1991-5010955	19911228
KR 9607532	B1	WO 1991-GB706	19910502
		KR 1991-702025	19911230
JP 11080153	A	JP 1991-508513	19910502
	Div ex	JP 1998-162127	19910502
JP 2927546	B2	JP 1991-508513	19910502
		WO 1991-GB706	19910502
JP 2000128787	A	JP 1998-162127	19910502
	Div ex	JP 1999-300923	19910502
TW 366346	A	TW 1992-102169	19910719
JP 3062475	B2	JP 1991-508513	19910502
	Div ex	JP 1998-162127	19910502
EP 1062950	A2	EP 1991-920963	19910502
	Div ex	EP 2000-118103	19910502
MX 193792	A	MX 1991-25621	19910502
US 6180639	B1	WO 1991-GB706	19910502
		US 1992-835964	19920220
CA 2059263	C	CA 1991-2059263	19910502



MARX 10/059,774

CA 2337748	A1 Div ex	WO 1991-GB706	19910502
		CA 1991-2059263	19910502
		CA 1991-2337748	19910502
CZ 288499	B6	CS 1991-1251	19910430
CN 1326743	A Div ex	CN 1994-109429	19910430
		CN 1999-126580	19910430
US 2003004175	A1 Cont of	US 1992-835964	19920220
		US 2001-771701	20010130

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 05501117	W	Based on	WO 9117159
HU 64335	T	Based on	WO 9117159
AU 651345	B	Previous Publ.	AU 9177719
		Based on	WO 9117159
EP 625150	A1	Based on	WO 9117159
NO 180377	B	Previous Publ.	NO 9200018
RO 112616	B1	Based on	WO 9117159
JP 2927546	B2	Previous Publ.	JP 05501117
		Based on	WO 9117159
JP 3062475	B2	Previous Publ.	JP 11080153
EP 1062950	A2	Div ex	EP 625150
US 6180639	B1	Based on	WO 9117159
CA 2059263	C	Based on	WO 9117159
CZ 288499	B6	Previous Publ.	CS 9101251
US 2003004175	A1	Cont of	US 6180639

PRIORITY APPLN. INFO: GB 1990-9861 19900502; WO 1991-GB706  
19910502

AN 1991-353701 [48] WPIX

AB WO 9117159 A UPAB: 20030416

(-)-Cis-4-amino-1- (2-hydroxymethyl-1,3 -oxathiolan-5-yl)-(1H)-pyrimidin-2-one (I) and its derivs. are new. (I) contg. max. 5 wt% of (+)-**enantiomer** (pref. below 1 wt%) is also claimed.

(I) is prepd. by sepn. from a racemic mixt., preferably by chiral HPLC. The stationary phase used is preferably beta-cyclodextrin or cellulose triacetate. Alternatively sepn. is by **enzyme**-mediated **enantioselective** catabolism, preferably using an immobilised **enzyme**. The **enzyme** is preferably cytidine deaminase or a 5-nucleotidase.

USE/ADVANTAGE - For treating viral infections (claimed). (I) is disclosed as being effective against HIV and having fewer side effects than AZT. (I) has the same activity vs. HIV as the (+)-**enantiomer** but considerably lower cytotoxicity. Suitable daily dosage is 1-20 mg/kg. (I) is also useful in treating AIDS related conditions, e.g. AIDS-related complex, progressive generalised lymphadenopathy, neurological conditions, anti-HIV antibody positive and HIV-positive conditions, Kaposi's sarcoma, thrombocytopenia purpura and associated opportunistic infections.

Administration can be oral, rectal, nasal, topical, vaginal or parenteral.

The antiviral activity of (I) was determined against C8166 cells infected with HIV-1 strain RF. by measuring inhibition of syncytium formation. The (-)-**enantiomer** gave an IC50 of 0.01 microg/ml compared to 0.05 microg/ml for the (+)-**enantiomer**.

ABEQ JP 05501117 W UPAB: 19930928

(-)-Cis-4-amino-1- (2-hydroxymethyl-1,3 -oxathiolan-5-yl)-(1H)-pyrimidin-2-one (I) and its derivs. are new. (I) contg. max 5 wt.% of (+)-**enantiomer** (pref. below 1 wt.%) is also claimed.

(I) is prepd. by sepn. from a racemic mixt., preferably by chiral HPLC. The stationary phase used is preferably beta-cyclodextrin or **enantioselective** catabolism, pref. using an immobilised **enzyme**. The **enzyme** is pref. cytidine deaminase or a 5-nucleotidase.

USE/ADVANTAGE - For treating viral infections (claimed). (I) is disclosed as being effective against HIV and having fewer side effects than AZT. (I) has the same activity vs. HIV as the (+)-**enantiomer** but considerably lower cytotoxicity. Suitable daily dosage is 1-20 mg/kg. (I) is also useful in treating AIDS related conditions, e.g. AIDS-related complex, progressive generalised lymphadenopathy, neurological conditions, anti-HIV antibody positive and HIV-positive conditions, Kaposi's sarcoma, thrombocytopenia purpura and associated opportunistic infections. Admin. can be oral, rectal, nasal, topical, vaginal or parenteral.

ABEQ ZA 9103293 A UPAB: 19930928

(-)-Cis-4-amino-1- (2-hydroxymethyl-1,3 -oxathiolan-5-yl)-(1H)-pyrimidin-2-one (I) and its derivs. are new. (I) contg. max. 5wt.% of (+)-**enantiomer** (pref. below 1 wt.%) is also claimed.

(I) is prepd. by sepn. from a racemic mixt., preferably by chiral HPLC. The stationary phase used is preferably beta-cyclodextrin or cellulose triacetate. Alternatively sepn. is by **enzyme-mediated enantioselective** catabolism, preferably using an immobilised **enzyme**. The **enzyme** is preferably cytidine deaminase or a 5-nucleotidase.

USE/ADVANTAGE - For treating viral infections (claimed). (I) is disclosed as being effective against HIV and having fewer side effects than AZT. (I) has the same activity vs. HIV as the (+)-**enantiomer** but considerably lower cytotoxicity. Suitable daily dosage is 1-20 mg/kg. (I) is also useful in treating AIDS related conditions, e.g. AIDS-related complex, progressive generalised lymphadenopathy, neurological conditions, Kaposi's sarcoma, thrombocytopenia purpura and associated opportunistic infections.

Administration can be oral, rectal, nasal, topical, vaginal or parenteral.

The antiviral activity of (I) was determined against C8166 cells infected with HIV-1 strain RF by measuring inhibition of syncytium formation. The (-)-**enantiomer** gave an IC50 of 0.01 microg/ml compared to 0.05 microg/ml for the (+)-**enantiomer**.

L50 ANSWER 14 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 1991-347643 [48] WPIX  
 DOC. NO. CPI: C1991-149849  
 TITLE: Ester(s) of (2R,3S)-3-(4-methoxy)phenyl-glycidic acid -  
 prepd. by **enantioselective enzymatic**  
 re-esterification of **enantiomer** mixts. of  
 another ester in presence of alcohol for diltiazem  
 prepn..  
 DERWENT CLASS: B03 D16  
 INVENTOR(S): FUGANTI, C; GENTILE, A; GHIROTTI, L; GIORDANO, C; SERVI,  
 S  
 PATENT ASSIGNEE(S): (ZAMB) ZAMBON SPA; (ZAMB) ZAMBON GROUP SPA  
 COUNTRY COUNT: 13  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4115697	A	19911121	(199148)*		
NL 9100854	A	19911216	(199202)		
SE 9101482	A	19911118	(199204)		
GB 2246351	A	19920129	(199205)		

FR 2662178	A	19911122 (199206)	
CA 2042535	A	19911118 (199207)	
GB 2247020	A	19920219 (199208)	
JP 04228095	A	19920818 (199240)	8
ES 2033203	A1	19930301 (199321)	
BE 1005406	A0	19930713 (199332)	18
CH 682670	A5	19931029 (199346)	
GB 2246351	B	19931215 (199350)	
GB 2247020	B	19931215 (199350)	
ES 2033203	B1	19931216 (199403)	
AT 9100995	A	19950515 (199525)	
IT 1249777	B	19950318 (199536)	
AT 400446	B	19951115 (199550)	
US 5571704	A	19961105 (199650)	5
CA 2042535	C	19980616 (199835)	
SE 509297	C2	19990111 (199908)	
JP 2000139492	A	20000523 (200033)	7
JP 3060187	B2	20000710 (200037)	7
DE 4115697	C2	20000907 (200043)	
JP 3223317	B2	20011029 (200171)	6
US 6346632	B1	20020212 (200219)	
NL 194616	B	20020501 (200237)	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4115697	A	DE 1991-4115697	19910514
NL 9100854	A	NL 1991-854	19910516
GB 2246351	A	GB 1991-110610	19910516
FR 2662178	A	FR 1991-5866	19910515
GB 2247020	A	GB 1991-20710	19910516
JP 04228095	A	JP 1991-210541	19910516
ES 2033203	A1	ES 1991-1193	19910516
BE 1005406	A0	BE 1991-458	19910516
CH 682670	A5	CH 1991-1329	19910503
GB 2246351	B	GB 1991-10610	19910516
GB 2247020	B Derived from	GB 1991-10610	19910516
		GB 1991-20710	19910516
ES 2033203	B1	ES 1991-1193	19910516
AT 9100995	A	AT 1991-995	19910514
IT 1249777	B	IT 1990-20348	19900517
AT 400446	B	AT 1991-995	19910514
US 5571704	A Cont of Div ex	US 1991-698853	19910513
		US 1994-197544	19940217
		US 1995-404284	19950314
CA 2042535	C	CA 1991-2042535	19910514
SE 509297	C2	SE 1991-1482	19910516
JP 2000139492	A Div ex	JP 1991-210541	19910516
		JP 1999-352154	19910516
JP 3060187	B2	JP 1991-210541	19910516
DE 4115697	C2	DE 1991-4115697	19910514
JP 3223317	B2 Div ex	JP 1991-210541	19910516
		JP 1999-352154	19910516
US 6346632	B1 Cont of Cont of	US 1991-698853	19910513
		US 1994-197544	19940217
		US 1995-487584	19950607
NL 194616	B	NL 1991-854	19910516

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AT 400446	B Previous Publ.	AT 9100995
JP 3060187	B2 Previous Publ.	JP 04228095
JP 3223317	B2 Previous Publ.	JP 2000139492

PRIORITY APPLN. INFO: IT 1990-20348 19900517

AN 1991-347643 [48] WPIX

AB DE 4115697 A UPAB: 19930928

Prepn. of esters of (2R,3S)-3-(4-methoxyphenyl) glycidic acid of formula (I) comprises re-esterifying enantiomer mixt. of (m)ethyl ester of (I), (i.e. (I; R = Me or Et) and their (2R,3S)-**enantiomers** (ent-(I)) **enantioselectively** and **enzymatically** using an alcohol which is different from that esterifying (I) and ent-(I)) and is of opt. branched 2-8C aliphatic- or 5-6C cycloaliphatic-alcohol or 2,2-dimethyl-1,3-dioxolan-4-methanol. The reaction is opt. carried out in the presence of pref. solvent (mixt.). The re-esterified ester (I) is sepd. from the unreacted ester. R = opt. branched 1-8C alkyl, 5-6C cycloalkyl or 2,2-dimethyl-1,3-dioxolan-4-methyl.

USE/ADVANTAGE - Intermediates in the synthesis of (+)-(2S,3S)-3-etharoyloxy -5-(2-(dimethyl amino)-ethyl)-2,3-dihydro -2-(4-methoxyphenyl) -1,5-benzothiazepin -4-(5H)-one (Diltiazem), a pharmaceutical with coronary vasodilatory properties. Pref. economically to separate the isomers in an early stage in the prodn. of Diltiazem i.e. to separate the (I)-isomers. The process gives (I) in good yields with high **enantiomer** purity, and also enables the undesired **enantiomer** to be recycled, racemising it, or reversing its configuration. The **enzyme** retains its **enzymatic** activity and can be used several times.

0/0

ABEQ BE 1005406 A UPAB: 19931118

Prepn. of esters of (2R,3S)-3-(4-methoxyphenyl) glycidic acid of formula (I) comprises re-esterifying **enantiomer** mixt. of (m)ethyl ester of (I), (i.e. (I; R = Me or Et) and their (2R,3S)-**enantiomers** (ent-(I)) **enantioselectively** and **enzymatically** using an alcohol which is different from that esterifying (I) and ent-(I)) and is of opt. branched 2-8C aliphatic- or 5-6C cycloaliphatic-alcohol or 2,2-dimethyl-1,3-dioxolan-4-methanol. The reaction is opt. carried out in the presence of pref. solvent (mixt.). The re-esterified ester (I) is sepd. from the unreacted ester. R = opt. branched 1-8C alkyl, 5-6C cycloalkyl or 2,2-dimethyl-1,3-dioxolan-4-methyl.

USE/ADVANTAGE - Intermediates in the synthesis of (+)-(2S,3S)-3-acetyloxy -5-(2-(dimethyl amino)-ethyl)-2,3-dihydro -2-(4-methoxyphenyl) -1,5-benzothiazepine -4-(5H)-one (Diltiazem), a pharmaceutical with coronary vasodilatory properties. Pref. economically to separate the isomers in an early stage in the prodn. of Diltiazem i.e. to separate the (I)-isomers. The process gives (I) in good yields with high **enantiomer** purity, and also enables the undesired **enantiomer** to be recycled, racemising it, or reversing its configuration. The **enzyme** retains its **enzymatic** activity and can be used several times. @ (6pp Dwg.No.0/0)@ Dwg.0/0

ABEQ GB 2246351 B UPAB: 19940203

A process for the preparation of an ester of (2R,3S)-3-(4-methoxyphenyl)-glycidic acid, the ester having the general formula I wherein R represents a linear or branched C1-C8 alkyl group, a C5-C6 cycloalkyl group or a 2,2-dimethyl-1,3-dioxolane-4-methyl group; the process comprising subjecting an **enantiomeric** mixture of (2R,3S) and (2S,3R)-3-(4-methoxyphenyl)-glycidic acid methyl ester or ethyl ester to

**enantioselective enzymatic** transesterification with an alcohol R'OH wherein R' has any of the meanings given above for R except a methyl group and is different from R and separating the transesterified ester from the untransesterified ester.

Dwg.0/0

ABEQ GB 2247020 B UPAB: 19940203

A process for increasing the **enantiomeric** purity of a non-racemic ester of 3-(4-methoxyphenyl)-glycidic acid in which the **enantiomeric** ratio (2R,3S):(2S,3R) is at least 80:20, the process comprising crystallising the ester from a solvent.

Dwg.0/0

ABEQ US 5571704 A UPAB: 19961211

A process for the preparation of esters of (2R,3S)-3-(4-methoxyphenyl)-glycidic acid of formula (I)

wherein R is a linear or branched C1-C8 alkyl group; a C5-C6 cycloalkyl group or a 2,2-dimethyl-1,3-dioxolane-4-methyl group; which consists of:

subjecting an **enantiomeric** mixture of (2R,3S)-3-(4-methoxyphenyl)-glycidic acid methyl ester or ethyl ester (I, R=CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>) and its (2S,3R)-**enantiomer** (ent-I) to an **enantioselective enzymatic** transesterification, in the presence of a **lipase** of animal or microbial origin as the **enzyme** and in the presence of an alcohol which is different from the alcohol esterifying compound I and ent-I and which is selected from the group consisting of a linear or branched C2-C8 aliphatic alcohol, a C5-C6 cycloaliphatic alcohol and 2,2-dimethyl-1,3-dioxolane-4-methanol, optionally in the presence of a suitable solvent or mixture of solvents; and

separating the transesterified ester from the untransesterified ester.

Dwg.0/0

L50 ANSWER 15 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1991-045737 [07] WPIX

DOC. NO. CPI: C1991-019353

TITLE: Prepn. of S-**enantiomer** of 1,3-dioxalane-4-methanol and derivs. - by subjecting **enantiomeric** mixt. to PQQ-dependent alcohol dehydrogenase.

DERWENT CLASS: B02 C02 D16

INVENTOR(S): DUINE, A J; GEERLOF, A; GROEN, B W; DUINE, J A; GROEN, B

PATENT ASSIGNEE(S): (STAM) STAMICARBON BV; (STAM) DSM NV

COUNTRY COUNT: 14

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 412585	A	19910213	(199107)*		
		R:	AT BE CH DE ES FR GB GR IT LI NL SE		
NL 8902035	A	19910301	(199113)		
DD 297161	A5	19920102	(199222)		
US 5182209	A	19930126	(199307)		7

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 412585	A	EP 1990-201651	19900625
NL 8902035	A	NL 1989-902035	19890809
DD 297161	A5	DD 1990-343334	19900808
US 5182209	A	US 1990-541910	19900622

PRIORITY APPLN. INFO: NL 1989-2035 19890809

AN 1991-045737 [07] WPIX

AB EP 412585 A UPAB: 19931129

A process for the **enantioselective** conversion of an **enantiomer** mixt. of 2R1, 2R2 - 1,3-dioxolane-4-methanol of formula (I) is claimed which comprises subjecting the **enantiomeric** mixt. to the action of an **enantioselective enzyme**, characterised in that a 2R1, 2R2-1,3-dioxolane-4-methanol enriched in S-**enantiomer** is prepd. by applying a suitable PQQ-dependent alcohol dehydrogenase (ADH) as **enantioselective enzyme**.

In (I) (R1, R2 = H, alkyl or aryl or R1 and R2 together with the C atom to which they are attached represent an opt. substd. carbocyclic ring).

Pref. the PQQ-dependent ADH originates from *Pseudomonas testosteroni* ATCC 15666, 15667, NCIB, 8893, NCIB 8955, NCIB 10808 or *Gluconobacter suboxydans* ATCC 621.

USE/ADVANTAGE - The PQQ-dependent ADH oxidises the R-**enantiomer** of (I) at a more rapid rate to form the S-**enantiomer** of the corresponding 2R1, 2R2-1,3-dioxolone-4-carboxylic acid, as a result of which also a reaction prod. enriched in S-2R1, 2R2-1,3-dioxolone-4-methanol is obtd. An **enantiomer** excess of more than 95% can be obtd. at a conversion of 50-55%. In a prefd. process an **enantiomer** excess of S-2,2-dimethyl-1,3-dioxolone-4-methanol (Ia) of at least 95% can be obtd. (Ia) can be used for the prepn. of pharmaceuticals, crop protection and/or agricultural pest control agents. It can also be used to prepare beta-receptor blocking agents and sn-glyceryl-phosphorylcholine. @(9pp DWg.No.0/1)@

ABEQ US 5182209 A UPAB: 19930928

**Enantioselective** conversion of an **enantiomeric** mixt. of 2R1, 2R2-1,3-dioxolane-4-methanol (I) comprises combining the **enantioselective enzyme** PQQ-dependent alcoholdehydrogenase with the mixt. where (I) is of formula (I) to produce mixt. of (I) enriched in S-(I). In the formula R1 and R2 are each H, opt. branched alkyl or aryl or CR1R2 forms an opt. substd. carbocyclic ring.

USE/ADVANTAGE - S-(I) is starting material for pharmaceuticals crop protection and/or agricultural pest control agents.

0/3

L50 ANSWER 16 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1990-297975 [40] WPIX

DOC. NO. CPI: C1990-128771

TITLE: Optical **resolution** of 1,3-dioxolane-4-carboxylate ester(s) - by **enantio-selective** hydrolysis with protease.

DERWENT CLASS: B03 D16 E13

INVENTOR(S): BOHME, M; DROESCHER, P; HAFNER, B; KNOLL, A; SCHICK, H G; SCHONECKER, R; SCHROTTER, E; SZYMANOWSK, M

PATENT ASSIGNEE(S): (BIOT-N) VE FORSCH BIOTECHNO

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DD 277698	A	19900411	(199040)*		

APPLICATION DETAILS:

MARX 10/059,774

PATENT NO	KIND	APPLICATION	DATE
DD 277698	A	DD 1988-322708	19881206

PRIORITY APPLN. INFO: DD 1988-322708 19881206

AN 1990-297975 [40] WPIX

AB DD 277698 A UPAB: 19930928

Prodn. of (5)-1,3-dioxolane-4-carboxylate esters of formula (I) is effected by treating the racemic cpd. with a proteolytic enzyme in the presence of a base, whereby the (R) isomer is selectively hydrolysed, and sepg. (I) from the (R) acid: In (I) R1 = alkyl, aryl or substd. benzyl; R2 = CH2, CH2CH2 (sic) or CR3R4; R3 and R4 = H, alkyl or aryl, or R3+R4 = (CH2)4 or (CH2)5.

USE/ADVANTAGE - (I) are useful as intermediates for natural prods., pharmaceuticals (e.g. steroids) and cosmetic prods. Process gives high yields (e.g. 44-83%) of (I) with high optical purity (ee = 34-87%).  
0/0

L50 ANSWER 17 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1990-291754 [39] WPIX

DOC. NO. CPI: C1990-125883

TITLE: New 1,3-dioxolane-4-methanol derivs. prodn. -  
by selectively hydrolysing racemic ester using carbonyl  
esterase.

DERWENT CLASS: B03 D16 E13

INVENTOR(S): BARNER, R; HUEBSCHER, J; WIRZ, B; HUBSCHER, J

PATENT ASSIGNEE(S): (HOFF) HOFFMANN-LA ROCHE AG; (HOFF) HOFFMANN LA ROCHE &  
CO AG F; (HOFF) HOFFMANN LA ROCHE INC

COUNTRY COUNT: 12

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 388778	A	19900926	(199039)*		19
R: AT BE CH DE FR GB IT LI NL					
JP 03215482	A	19910920	(199144)		
EP 388778	A3	19920102	(199320)		19
US 5232852	A	19930803	(199332)		
US 5283346	A	19940201	(199406)#		8
EP 388778	B1	19960110	(199607)	GE	23
R: AT BE CH DE DK FR GB IT LI NL					
DE 59010041	G	19960222	(199613)		
JP 3012273	B2	20000221	(200014)		16

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 388778	A	EP 1990-104859	19900315
JP 03215482	A	JP 1990-67386	19900319
EP 388778	A3	EP 1990-104859	19900315
US 5232852	A	US 1990-492166	19900313
US 5283346	A Div ex	US 1990-492166	19900313
		US 1992-990231	19921214
EP 388778	B1	EP 1990-104859	19900315
DE 59010041	G	DE 1990-510041	19900315
		EP 1990-104859	19900315
JP 3012273	B2	JP 1990-67386	19900319

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5283346	A Div ex	US 5232852
DE 59010041	G Based on	EP 388778
JP 3012273	B2 Previous Publ.	JP 03215482

PRIORITY APPLN. INFO: CH 1989-1093 19890323

AN 1990-291754 [39] WPIX

AB EP 388778 A UPAB: 19940303

(A) 1, 3-Dioxolane-4-methanol derivs. of formula (I) are new: Where R1 and R2=Me or Et, or R1+R2=(CH2)5; R3=H, 2-9C alkanoyl, alkylsulphonyl or arylsulphonyl; provided that (a) R3 is not H when R1=R2=Me, and (b) the cpds. are chiral when R1+R2=(CH2)5 and R3=H (B) Prodn. of optically active 1, 3-dioxolane-4-methanol derivs. of formula (Ia') and (Ib') is effected by selectively hydroglysing a racemic ester of formula (Ia) using a carboxyl **esterase**, triacylglycerol **lipase**, cholesterol **esterase** or diacylglycerol **lipase enzyme**: (R3'=2-9C alkanoyl). (C) Prodn. of d-alpha-tocopherol (II) is effected by: (a) converting (Ib') to the corresp. (R)-alkylsulphonate or (R)-arylsulphonate, removing the protecting gp. CR1R2 and converting the resulting (R)-diol to (II) in known manner; or (b) hydrolysing (Ia') to obtain the (R)-alcohol (Ib''), converting this to the corresp. (A)-alkylsulphonate or (S)-arylsulphonate, removing the protecting gp. CR1R2, and converting the resulting (S)-diol to (II) in known manner.

USE - (II) is an active form of vitamin E. @(19pp Dwg.No.0/0)@  
0/0@

ABEQ EP 388778 A UPAB: 19930928

(A) 1, 3-Dioxolane-4-methanol derivs. of formula (I) are new: Where R1 and R2=Me or Et, or R1+R2=(CH2)5; R3=H, 2-9C alkanoyl, alkylsulphonyl or arylsulphonyl; provided that (a) R3 is not H when R1=R2=Me, and (b) the cpds. are chiral when R1+R2=(CH2)5 and R3=H (B) Prodn. of optically active 1, 3-dioxolane-4-methanol derivs. of formula (Ia') and (Ib') is effected by selectively hydrolysing a racemic ester of formula (Ia) using a carboxyl **esterase**, triacylglycerol **lipase**, cholesterol **esterase** or diacylglycerol **lipase enzyme**: (R3'=2-9C alkanoyl). (C) Prodn. of d-alpha-tocopherol (II) is effected by: (a) converting (Ib') to the corresp. (R)-alkylsulphonate or (R)-arylsulphonate, removing the protecting gp. CR1R2 and converting the resulting (R)-diol to (II) in known manner; or (b) hydrolysing (Ia') to obtain the (R)-alcohol (Ib''), converting this to the corresp. (A)-alkylsulphonate or (S)-arylsulphonate, removing the protecting gp. CR1R2, and converting the resulting (S)-diol to (II) in known manner.

USE - (II) is an active form of vitamin E.  
0/0

ABEQ US 5232852 A UPAB: 19931118

Prodn. of s-enantiomer of an alcohol of formula (I) comprises enzymatic hydrolysis of the racemic cpd. using **lipase**

-P-30, **lipase** SAM, **lipase** PM, **lipase** LMM,

**lipase** 2RD, **lipase** D, **lipase** LRA,

**lipase** CE, **lipase** FAP or **lipase** MAP, and

recovering the s-enantiomer in (I) R, and R2 are independently Me or Et or R1+R2 form pentamethylene.

USE/ADVANTAGE - (I) are intermediates for vitamin E esp. in its optically active form d-alpha-tocopherol. The **lipase** is pref. of microbial origin from Pseudomonas fluorescens, Mucor mehei, Rhizopus delemar, Rhizopus arrhizus, etc. (17pp Dwg.No.0/0)



ABEQ US 5283346 A UPAB: 19940322

**Diox lanes** of formula (Ia) and (Ic), racemates and **enantiomers**, are new. In the formulae, R1 and R2 are independently Me or Et or together form pentamethylene; R3' is 2-9C alkanoyl; p R3'' is alkane- or aryl-sulphonyl.

Specifically claimed cpds. include ((R,S)-2-methyl-2,4-dioxaspiro-(4,5)-dec-2-yl) methyl butyrate. **Enantiomers** are obtd. by **enzymatic** hydrolysis of the corresp. (R,S) alkanolic acid ester.

USE/ADVANTAGE - Intermediates to Vitamin E.

Dwg.0/0

ABEQ EP 388778 B UPAB: 19960222

A process for the manufacture of a compound of the general formula (I) or (II), wherein R1 and R2 each independently signify methyl or ethyl or together signify pentamethylene, characterised by hydrolysing a racemic alkanolic acid ester of the general formula (III), wherein R1 and R2 have the significances given above and R3 signifies C2-9-alkanoyl, to the compound of general formula (I) using an **enzyme** of the sub-class carboxyl **esterases** (EC 3.1.1.1), triacylglycerol **lipases** (EC 3.1.1.3), cholesterol **esterases** (EC 3.1.1.13) or diacylglycerol **lipases** (EC 3.1.1.34) or hydrolysing the (S)-alkanoic acid ester of the general formula (IV), wherein R1, R2 and R3' have the significances given above, which does not react when the **enzymatic** hydrolysis is carried out, to the corresponding (R)-alcohol of the general formula (V), wherein R1 and R2 have the significances given above.

Dwg.0/0

L50 ANSWER 18 OF 19 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1990-201019 [26] WPIX

DOC. NO. CPI: C1990-087056

TITLE: Optically active glycerol ketal ester derivs. prepn. - by **resolution** of racemic ester with **enzyme** from Streptomyces parvulus or Micrococcus luteus.

DERWENT.CLASS: B03 D16

INVENTOR(S): SIH, C J

PATENT ASSIGNEE(S): (WISC) WISCONSIN ALUMNI RES FOUND

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4931399	A	19900605	(199026)*		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4931399	A	US 1985-773493	19850909

PRIORITY APPLN. INFO: US 1985-773493 19850909

AN 1990-201019 [26] WPIX

AB US 4931399 A UPAB: 19930928

Method for **resolving** racemic 2,3-O-substd. glycerol esters comprises treating the esters with **enzymes** produced by Streptomyces parvulus ATCC 19796 or Micrococcus luteus ATCC 9341 and recovering optically active 2,3-O-substd. glycerol and optically active 2,3-O-substd. glycerol esters.

The esters are treated with **enzymes** produced during

cultivation in aq. nutrient medium under submerged aerobic conditions, pref. at 10-35 deg C for 12 hrs - 10 days, pref. using immobilised cells; or by exposure to the isolated **enzymes**, pref. immobilised. Prefd. esters are 2-4C acyl ester of 2,2-dimethyl-or 2,2-pentamethylene-1,3-dioxolane-4-methanol.

USE/ADVANTAGE - The chiral prods. are useful as intermediates in synthesis of chiral beta-adrenergic blocking agents for treatment of heart disease, hypertension, glaucoma, etc.; of phospholipids; of platelet activating factor; and of chiral mono-, di- and tri-glycerides.

O/O

L50 ANSWER 19 OF 19 WPIX (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 1988-088330 [13] WPIX  
 DOC. NO. CPI: C1988-039619  
 TITLE: Optical method of sepg. pentagonal cyclic alcohol - using glucose-transferase and 6-substd. sucrose deriv. to prepare separable diastereomer.  
 DERWENT CLASS: B04 D16  
 PATENT ASSIGNEE(S): (MITD) MITSUI SUGAR CO LTD.  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 63039590	A	19880220	(198813)*		6
JP 2597995	B2	19970409	(199719)		5

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 63039590	A	JP 1986-183376	19860806
JP 2597995	B2	JP 1986-183376	19860806

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 2597995	B2 Previous Publ.	JP 63039590

PRIORITY APPLN. INFO: JP 1986-183376 19860806

AN 1988-088330 [13] WPIX

AB JP 63039590 A UPAB: 19930923

The method relates to the optical dividing method for pentagonal cyclic alcohol and is characterized by (a) using glucosyltransferase, 6'-substd. sucrose deriv. as glucosyl donor and pentagonal cyclic alcohol as glucosyl acceptor and (b) hydrolysing the glucoside bond of formed glucosylated cpd. either as it is or in the case that the glucosylation lacks the selectivity for optical **enantiomer**, after sepg. diastereomer from reaction product.

As pentagonal cyclic alcohol, pentagonal cyclic **dioxolan**, pentagonal cyclic tetrahydrofuran and pentagonal cyclopentane can be used favourably. As hydrolysing **enzyme** alpha-glucosidase can be used and alpha-glucosidase and sucrose glucosyltransferase may be used in the form of fixed **enzyme**.

USE/ADVANTAGE - By the method, pentagonal cyclic alcohol can be optical divided and thus divided optical active pentagonal cyclic alcohol can be used widely as the material for synthesizing various physiologically active substances such as prostaglandin, glycerolipid, pheromone, etc.

MARX 10/059,774

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